VOL. II, No. 4 APRIL-JUNE

Acta Medica Philippina

Published Four Times a Year
by the
COLLEGE OF MEDICINE
and the
INSTITUTE OF HYGIENE

MANILA
PHILIPPINES
1941

ACTA MEDICA PHILIPPINA

Published by the College of Medicine and the Institute of Hygiene, University of the Philippines

Entered as second class matter at the Manila Post Office on October 5, 1939

ACTA MEDICA PHILIPPINA

Publication Office: Institute of Hygiene, University of the Philippines, Manila, Tel. 5-72-27 or 5-64-06

VOL. II APRIL-JUNE No. 4

Clinical Medicine:

Clinical Pathology:

Chemical Hygiene and Nutrition:

Parasitology:

TYPHUS FEVER: SOME UNUSUAL CLINICAL MANIFESTATIONS *

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The presence of typhus fever in the Philippine Islands has long been noted, having been repeatedly mentioned in annual reports of the Philippine Bureau of Health (1912-1914). The first work "to show unquestionably that endemic typhus exists in the Philippines" was that of Foster [1] who reported twenty-three cases found in Camp Keithley, Lanao. The diagnosis was based mainly on the symptomatology alone so that mild or atypical cases must have been missed. In 1937 by means of the Weil-Felix reaction, Roda [2] showed definitely the prevalence of typhus fever and temporarily set the diagnostic titer of the test at 1:500 or over, lower titers having been found of doubtful value.

In a period of three and a half years, we have collected nine cases of typhus fever in the student body of the University of the Philippines. In arriving at a diagnosis, we did not depend only on a certain group of symptoms, but also on a positive Weil-Felix reaction. No two of our cases came from the same household and none gave a history of contact with a typhus fever patient. These patients were placed in the general ward and no special preventive precautions were observed; yet there was no outbreak of an epidemic. Our cases, therefore, seemed to belong to the group designated by Fletcher and Lesslar [3] as "tropical typhus fever", a "group although identical in symptoms with the classical or epidemic typhus, is characterized by its low infectivity—its transfer from one person to another being doubtful—and by its prevalence in the tropics." [3]

This paper will set forth certain unusual clinical manifestations met with in some of the nine cases of typhus fever. At-

* Read at the 38th Annual Convention, Philippine Medical Association, April 22, 1941.

tention is drawn to this direction because of the belief that the clinician may meet with these manifestations in similar cases occurring in the Philippines, without recognition of their real etiology.

While the onset, as a rule, was usually sudden, beginning as fever with joint or muscular pain, chilly sensation, headache of varying degree or catarrhal symptoms, yet the initial features of some might cause confusion. One of the nine cases in this review had a rather slow onset and the patient continued attending his classes for almost a week. Another was admitted due to the complaints of fever and purulent discharge from the left ear. Still another began as fever, cough and backache and on physical examination showed the classical signs of effusion, right. Others complained only of fever, headache and joint or muscular pains, highly simulating influenza. None had actual chills, although almost all had chilly sensations. One had repeated epistaxis, the others had catarrhal symptoms.

The incubation period could not be determined in this study. Yersin and Vassal,[4] by direct inoculation of 0.5 cc. of which blood from a typhus fever patient into healthy individuals, were able to reproduce the disease in two instances after a period of fourteen and twenty-one days, respectively.

In their study of the 1920 typhus epidemic in Poland, the Typhus Research Commission of the League of Red Cross Societies[5] stated that "among our cases evidence of tracheobronchitis was so prevalent as to lead us to believe it characteristic of the disease as with measles." At autopsy, they found some degree of bronchitis and bronchopneumonia in nearly all cases. However, they could find no changes attributable to typhus fever in the serous endothelium, especially the pleura. Although none of our studied cases developed bronchopneumonia, one had right-sided pleural effusion.

An abstract of the clinical history of this patient follows:

> A twenty-year-old male was admitted on Feb. 9, 1939 due to fever, cold, and headache which began two days previous to admission. On the sixth day, he had impairment of resonance at the right base with slightly diminished breath sounds but no rales. On the tenth day, the impairment of resonance was more marked, breath sounds more

distant but still no rales. On the eighteenth day the above findings disappeared and the fever subsided. The total leucocyte and differential counts were normal and blood culture remained sterile after seventy-two hours. Urinalysis was negative. Radiography of the chest was unsatisfactory as the picture was taken with the patient in recumbent position. The tentative diagnosis was pleurisy with effusion, right, but when the physical signs disappeared with the fever on the eighteenth day of illness and with a positive Weil-Felix reaction, we revised our original impression, believing that the effusion was probably but a manifestation of typhus fever.

Ear complications, as otitis media, were not infrequent among eruptive fevers, according to Cecil.[6] However, Wolbach, Todd and Palfrey [5] encountered only four cases with ear complications during the 1920 typhus epidemic in Poland. We observed it in only one case, apparently the first one recorded locally complicating typhus fever.

A summary of the clinical history of the case follows:

A seventeen-year-old male, was admitted on October 30, 1939 complaining of fever and pain in the left ear. The onset came suddenly three days previously. On the second day the fever rose and there was some foul discharge from the left ear canal. On the fourth day the pain subsided and the discharge ceased. On the tenth day he felt slight pain in the other ear and two days later there was purulent discharge from the right ear canal. The drum membranes were congested and showed pin-point perforations without sagging or pulsation. There were several enlarged cervical lymph glands. Throughout his illness, he complained of severe headache. Laboratory examinations showed normal total and differential counts, notwithstanding the bilateral middle ear infection. Blood culture was sterile after seventy-two hours. Urinalysis revealed slight traces of albumin. The Weil-Felix reaction on the twelfth day was strongly positive. Two days later the patient was afebrile, with clearing of both ears.

In classical typhus fever nervous symptoms have been very prominent features. Nearly all cases reported by Musgrave

and Sison 7 "were characterized by a period of delirium of a maniacal character". One of our nine cases had persistent insomnia, another had severe headache and still a third had some mental dullness. The other patients complained only of slight or moderate headache and mild insomnia such as is encountered in other fevers. None showed mental excitement, active delirium or meningeal symptoms as described by Cecil.

The following is a brief case report with fever and persistent insomnia as main manifestations:

> A twenty-year-old male was admitted on July 12, 1940 due to fever and colds. Nine months previously he had left-sided acute interstitial pneumonitis. The present illness started on the eve of admission as fever, headache and cough following exposure to rain. Cough was dry and occasional; there was neither chill, chest pain nor backache. During his stay in the ward, he complained of persistent inability to sleep despite administration of sleeping tablets. Physical examination on admission revealed only slight congestion of the pharyngeal vault. Later he developed moist rales at both bases especially the left. Facies was bright in spite of the fever. Blood examination showed normal total and differential counts. Urine had traces of albumin. Blood culture was sterile after seventy-two hours. Sputum was repeatedly negative for acid-fast bacilli. Radiogram of the lungs showed no definite evidence of tuberculosis. At the end of the second week the fever came down and suspicion of typhus fever was confirmed by a positive Weil-Felix reaction.

The most prominent gastro-intestinal manifestation observed was obstinate constipation in seven cases. Wolbach, Todd and Palfrey 5 wrote "constipation was the rule throughout although diarrhea was present in 17 cases". Cecil found vomiting and diarrhea, especially during the height of the disease, as the most common gastro-intestinal symptoms. That obstinate constipation instead of diarrhea or vomiting was the striking gastro-intestinal feature in our series may have been due to mildness of the infection.

Skin eruptions were observed only in three of the nine cases. The exanthem appeared especially on the chest, back and

neck as non-elevated, rounded, pin-head, or slightly larger, maculo-papular eruptions which disappeared on pressure. In one case it appeared on the third day, in another on the fifth day, while in a third case, on the seventh day. We have not seen the hemorrhagic type of eruption.

The temperature curve in our cases roughly corresponded with that of typhoid fever. Total duration did not exceed two weeks save in one case. We were fortunate in getting hold of the patients on the second or third day of illness. On admission, the temperature was usually about 39°C., was irregular but slightly remittent for two or three days (chart 1), and from the fifth or sixth day, it remained high for four or five days more (chart 2) with very mild remissions, the last phase probably corresponding with the period of fastigium in typhoid fever.

After the tenth or twelfth day the temperature showed a tendency to become irregular again, finally ending either in crisis (chart 5) or rapid lysis (charts 1 to 4). In some instances, the temperature curve ended in slow lysis (chart 6).

The blood picture was not diagnostic. The total leucocytic count varied from 4,200 to 10,600 per cu. mm. The neutrophiles ranged from 38% to 80% with an average of 64.6%. The combined small and large lymphocytes varied from 18% to 56% with an average of 31.5%. It would appear as if there was a tendency to slight lymphocytosis.

The superficial lymphoid tissue was slightly enlarged in most of the cases especially the cervical, axillary, and the inguinal groups of lymph glands. They were either palpable, non-tender or only slightly so, discrete and with no tendency to suppurate. Neither the liver nor spleen was palpable in any of the cases.

COMMENT

Clinically simulating influenza, mild cases of "tropical typhus fever" may be missed readily unless the Weil-Felix reaction is performed. Cases with unusual manifestations—or "complications"—as otitis media or pleurisy with effusion, may be taken merely as such, the real etiology possibly remaining unrecognized.

In the matter of care and treatment, there being no specific drug for typhus fever, only symptomatic therapy has been employed in these cases. Sulphanilamide administered to the cited case presenting otitis media yielded no encouraging result for neither did it shorten the duration nor did it prevent the involvement of the opposite ear.

As for food, light nourishing diets were given in most cases save in the cited case with persistent insomnia, who was allowed to have no dietary restriction. In this patient, neither dehydration nor toxicity was observed to occur.

SUMMARY

The striking unusual manifestations noted in nine studied cases of typhus fever among the student body of the University of the Philippines during a period of three and a half years, yielding strongly positive Weil-Felix reactions, were: obstinate constipation in seven cases; successive bilateral otitis media in one; pleurisy with effusion, one; persistent insomnia, one; and repeated epistaxis, one. The exanthem was noted only in three of nine cases.

Nervous manifestations, as a whole, were mild. So was the infection itself, as all nine cases recovered.

The temperature curve roughly resembled that of typhoid fever. The duration, except in one case, did not exceed two weeks.

The mild nature of the infection suggested that the studied cases might have been instances of "tropical typhus fever" after Fletcher and Lesslar.[3]

Without the confirmatory Weil-Felix test, cases of typhus fever in the Philippines may be mistaken easily for influenza. Those with manifest otitis media or pleurisy with effusion, as cited herewith, may be readily taken likewise for these conditions.

ACKNOWLEDGMENT

Acknowledgment is due Dr. Alfredo Pio de Roda of the Institute of Hygiene, University of the Philippines, for performing the Weil-Felix reactions.

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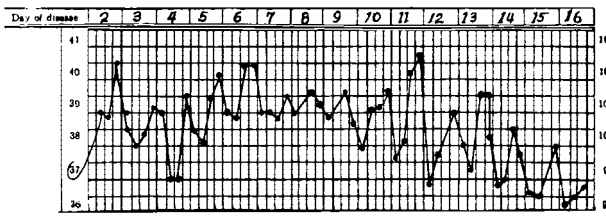

Chart 1. The temperature remained high with very slight remission for four days. Patient presented no characteristic symptoms.

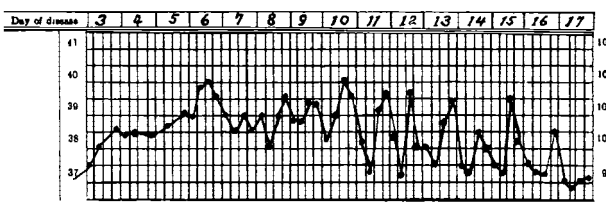

Chart 2. From the seventh to tenth day the temperature curve had very slight remission. Patient had mental dullness and severe headache.

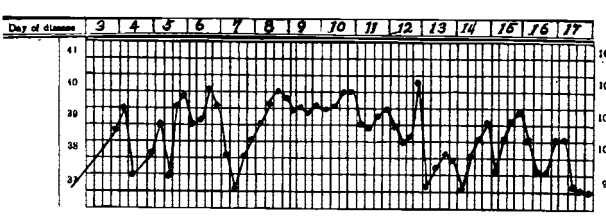

Chart. 3. From the eighth to the twelfth day, the temperature remained more or less constant. Patient had pleural effusion, right.

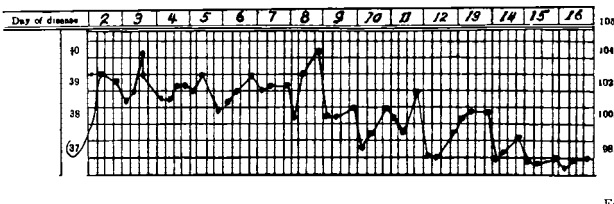

Chart 4. Patient had persistent insomnia. The temperature ended in rapid lysis.

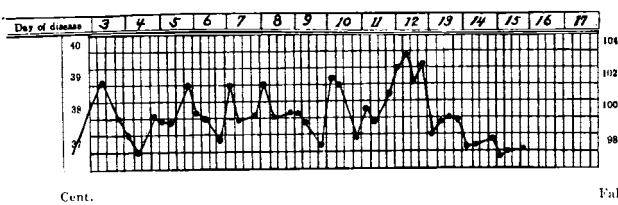

Chart 5. Patient had purulent otitis media as reported above. The temperature ended in crisis.

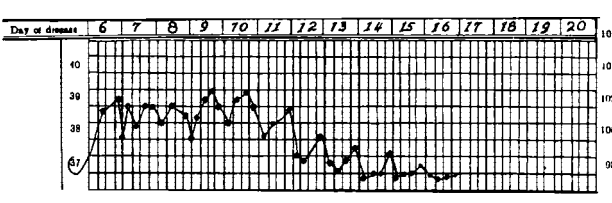

Chart 6. Here the temperature came down very gradually. Onset was slow and patient continued attending classes for a week. Repeated epistaxis was the striking feature.

THE ROENTGEN TREATMENT OF OPERATED BREAST CARCINOMA

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(Director: PROF. DR. H. HOLFELDER)

One of the most frequent sites of carcinomatous lesions is the breast. Therefore a good knowledge of the proper manner of radiation of breast carcinoma is very essential.

The ideal way of treating mammary carcinoma is to operate as early as possible and then use prophylactic radiation. However there are cases which come for radiological treatment which have not been operated, either because of clinical or technical inoperability or because of the tenacious fear of the patient for anything surgical. In this condition another method of radiation is given according to the requirements of the case. In this article however I shall confine the discussion to the radiological treatment of cases that have been operated upon.

The principle of treatment is to give all over the breast in question a homogenous dose of 2 HED or 1100 r (measured in air) distributed over 8 to 10 days as follows:

Days	1	2	3	4	5	6	7	8
Herd-	80%		40%		40%			40%
Dosis	(440 r)		(220 r)		(220 r)			(220 r)

(Note: 100% of HED = 1 U.S.D. = 550 r unit measured in air)

The problem is to find a way by which we could give such a working dosage without, at the same time, giving unnecessary radiation to the normal tissues as the lungs. The breast from the lateral sternal border of the opposite side to the posterior

axillary line of the affected side must be homogenously radiated at a depth that will include the whole breast wall avoiding as much as possible the lung tissue. To accomplish this, a tube of 20×24 is needed, arranging it in such a way that it is more or less tangential to the curvature of the breast and using only a part of the peripheral rays passing through the tube (fig. 1 and 2). This arrangement however will make the radiation on the superficial portion of the breast not of the same working conditions as those in the deeper part because of the lack of secondary radiation. To remedy this, rice or bollus sacks are laid to give the necessary homogeneity of radiation from the skin to the deeper part of the chest wall.

But with the use of lateral (posterior axillary) and medial (sternal) fields alone the doses at the middle of the breast are still not enough to make the radiation of the entire breast perfectly homogenous. Hence the use of the so-called supplementary field is needed. Here the Roentgen rays are allowed to pass thru a wedge-shaped lead diaphragm so as to permit only that amount of radiation to pass as is necessary to compensate for the gradual diminution of dosage from the periphery to the center as given from the lateral and medial fields. Thus with this device the problem of homogeneity is solved. As we will notice it is only in the supplementary field where radiation is given perpendicular to the breast (fig. 3). And even here the quantity of rays allowed to pass thru the wedge-shaped lead diaphragm that may reach the lung is too insignificant to produce any pulmonary injury or general intoxication.

In the treatment of post-operated mammary carcinoma the regional lymphatic glands should receive due attention. The axillary and supraclavicular regions must be radiated during the interval between mammary radiations.

To illustrate, we could have the following scheme:

PROPHYLACTIC RADIATION OF OPERATED MAMMARY CARCINOMA

Days	Sternal field	Supplementary field	Lateral field	Supraclavicular field	Axillary field	Herd Dosis
1	60% (330r)	20% (110r)	60% (330r)			80% (440r)
2				60% (330r)		
3	30% (165r)	10% (55r)	30% (165r)			40% (220r)
4					60% (330r)	
5	30% (165r)	10% (55r)	30% (165r)			40% (220r)
6				60% (330r)		
7					40% (220r)	
8	30% (165r)	10% (55r)	30% (165r)			40% (220r)
9				40% (220r)		
10					40% (220r)	
11				40% (220r)		
Total				200% (1100r)	140% (770r)	200% (1100r)

The 60%, 20%, 60% (330 r, 110 r, 330 r) dosis for the sternal, supplementary, and lateral fields respectively to give a homogenous dose of 80% or 440 r will depend upon the constitutional build of the breast to be treated. The method of calculation is illustrated in fig. 4 and a radiologist familiar with the use of Prof. Holfelder's anatomical cross-section and field selectors will easily understand the point.

A tube of 8 × 10 is usually used in the radiation of the supraclavicular and axillary regions. The dose given the axillary area is a little less than the supraclavicular part because it

is to be noted that during the radiation of the lateral (post. axillary line) field the axillary fossa is already receiving part of it.

The second series of application may be given three or four to five months after and the third, six to seven months after the second. It is to be remembered, however, that the number and interval between series of application of radiation must be guided by the clinical aspect and skin reaction of the individual patient.

The ingenuity, practicability, and effectiveness of this HOLFEDERIAN method of treatment is very apparent when we see the following statistics.

Of 115 cases treated in the University Roentgen Institut 79 were able to live for at least 5 years giving a percentage 5 years cure of 68.69%, while with surgical treatment alone Scandinavian surgeons give the following statistics:

Percentage of 5 years cure by surgical treatment alone of cancer of the breast in Scandinavia

Author	Dahlgren	Neander	Brottstorm	Nystrom	Surala	Kalima
Percentage of 5 years cure	15%	16.8%	25.5%	21.5%	18%	24%

Comparing the two results we could easily appreciate the important role played by modern Roentgen therapy, if wisely given, in the treatment of such cases.

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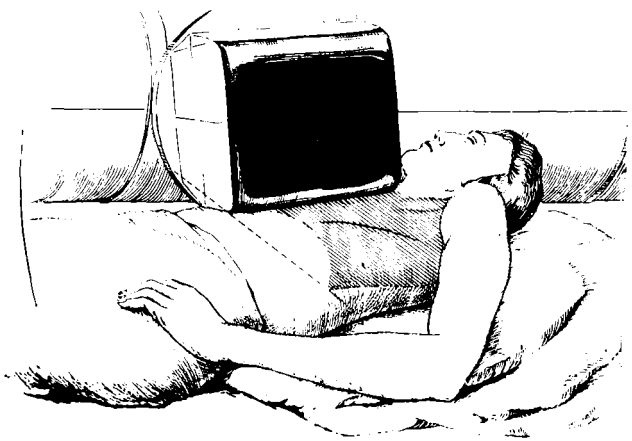

FIG. 1.
Radiation of the sternal field.

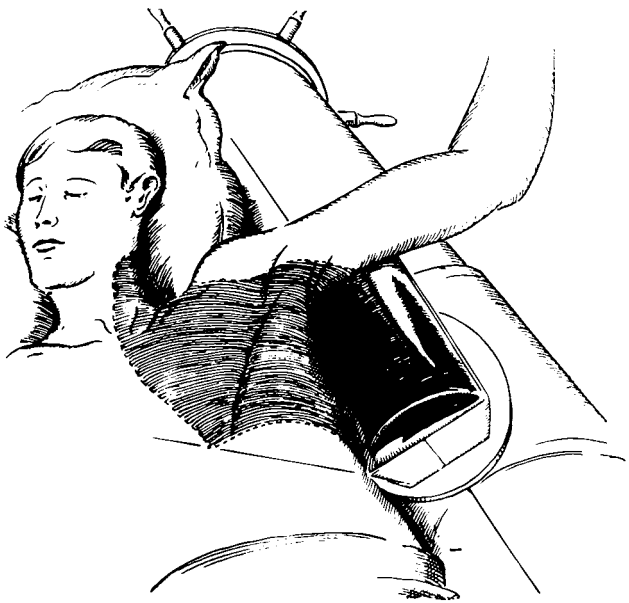

FIG. 2.
Radiation of the lateral field.

FIG. 3.
Radiation of the supplementary field

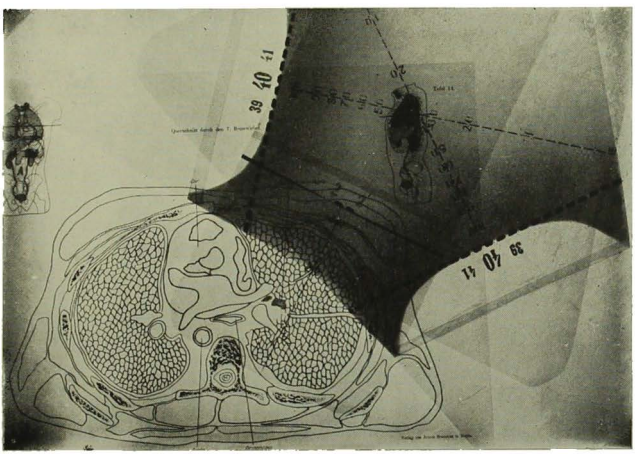

FIG. 4.

Showing the use of Prof. Holfelder's anatomical cross-section and field selectors for the calculation of dosage of the part to be treated.

AUTO-UROTHERAPY IN URTICARIA *

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Urticaria, like all allergies, have up to the present time defied all the therapeutic resources which physicians have at their disposal. Altho the disease is not serious and per se not fatal, it still remains one of those conditions which are productive of symptoms annoying enough to merit the physician's concern.

The futility of the varied forms of treatment in urticaria is in all probability due to our meager knowledge of the real nature of the condition. We call it allergy, we surmise about the mechanism of its production, we try the ordinary routine of treatment for all allergies—but we should confess that we still have not solved the mystery that veils the true mechanism of urticaria and all allergies in general.

For our purpose, it maybe worthwhile naming the different factors which are known to cause urticaria. Just how it is really brought about, we can not exactly tell at the present time. The proposed theories and mechanism of its production are as varied as our approach to the treatment of the condition. Such multiplicity is only an indication of our meager knowledge.

The causes of urticaria as are known at the present time may be grouped under the following headings:

1. Gastro-intestinal. Under this group may be placed all allergens which are taken in by way of the gastro-intestinal route. They are usually in the form of food, either vegetable, animal, or inorganic in origin. There are legions of them, but the most common offenders, as far as we have observed in our cases, are sea foods, beef and pork products, fowls and rarely vegetables. Under this group may also be included some beverages, and medicinal agents which in susceptible individuals produce urticaria. Most of our cases fall under this group.

* Read at the 38th Annual Convention, Philippine Medical Assocation, April 24, 1941.

2. Parenteral. Under this heading falls the less common cause of urticaria which is brought about usually as a result of our treatment of some disease or condition. To this group belong a number of drugs, foreign proteins, immune serums, blood, vaccines, and other biological products which are administered parenterally, namely, percutaneously, hypodermically, intramuscularly, intravenously etc.

This group, however, has only a passing importance as far as our form of therapy is concerned since the reaction is easy to control and its repetition can be avoided by simple precautionary measures.

3. Environmental. This group comprises those factors which may be thermal, chemical, climatic, and other environmental conditions which may affect us untowardly. There are only a few cases belonging to this group. An example of this group is urticaria brought about by an early morning bath. This group presents no problem on account of its rarity and the fact that it is easily avoidable.

4. Endocrinologic. This group comprises those yet unknown disturbances of the endocrine glands to which human being is heir. Our knowledge of endocrinology is yet meager, just as meager as our knowledge about the mechanism of urticaria in such cases. Under this group may also be included those cases of urticaria brought about by emotional upsets. Fortunately enough there are only few cases directly attributable to such factors.

5. Infectious or Toxemic. This group comprises the different toxemias and infections which cause urticaria. Well known is the observation, altho not common, of some infections and intoxications being able to produce urticarial eruptions. The condition, however, is no problem to us, as our main concern in these cases is the treatment of such infections or intoxications. As we all see, if we know the exact cause, therapy becomes obvious.

6. Mixed Group. This group comprises a combination of two or more of the above causes.

7. Unknown Group. This includes all those causes of which we know nothing; this probably comprises one of the largest groups.

As is common knowledge, the majority of cases of urticaria that comes to the physician is traceable to certain kinds of food or food products. In our cases, the majority gives a history of the attacks subsequent to the taking in of sea foods, beef and pork, fowls, and some beverages like beer. It is to be noted that as a rule patients do not react to only one kind of food but usually to many.

An inquiry into the family history of the patients revealed that in most cases there are certain evidences of hypersensitiveness in the ascendants or descendants. They are in the form of bronchial asthma, eczema, urticaria, vasomotor rhinitis, or a combination of these. This is in accord with the observation of many investigators that allergy has some familial tendencies.

Specific tests for hypersensitiveness were done in some cases in 1934 and 1935. The test consisted in applying stock protein extracts to scarified areas on the flexor surfaces of the forearms, and formation of erythema and slight edema within twenty four hours which persisted for a day or two was taken as a positive test. Control areas with normal saline were made for comparison. We, however, did not use this test as we found out that all the cases responded to a group of allergens, and that no single case reacted to one single allergen.

The idea in making the above test is to know the specific cause so that we may institute specific procedures of desensitization. The fact that there are so many allergens to which the patient is a reactor made such a procedure not feasible.

PROCEDURE OF TREATMENT

Cases who came with the urticarial eruptions were right away given auto-urotherapy. Those cases who had a history of the eruption, but did not show actually the eruptions were told to come back when they had them, in order to be sure that we were not dealing with some other condition.

Briefly, the procedure consists in reinjecting to the patient his freshly voided urine which is aseptically collected and sterilized. The complete technic is as follows;

1. The patient, properly advised, is made to urinate into a sterile receptacle, say, a kidney basin, discarding the

first flow to allow for mechanical cleansing of the lower urinary passage.

2. The urine is treated with iodized alcohol prepared by dissolving one gram of iodine crystals in 100 cc. 70% alcohol. The proportion is one drop of the iodized alcohol to 1 cc. of urine to be injected, adding a drop or two in excess to allow for a thorough sterilization.

3. The mixture is sucked in the syringe many times to allow for a thorough mixing, then allowed to stand for a few minutes to permit the sterilizing action of the iodine.

4. The treated urine is injected hypodermically or intramuscularly (for doses higher than 2 cc.) beginning with 0.5 cc. or 1 cc., increasing by multiples of 0.5-1 cc. Smaller doses are given to children. Injections are preferably given every other day. Five injections constitute a course.

5. A rest interval of one week is given, then the injections are resumed. A few cases required a continuation of treatment without the rest interval.

6. While the injections are being given, the patients are told to eat the foods which they have observed to bring on the attack. Injections are continued until such a time is reached when the previously offending foods no longer evoke a reaction. No other forms of treatment were instituted.

REPORT OF CASES

There are 41 cases in all. Of these 18 are private cases, the rest are dispensary patients.

Of the private cases, the duration of the condition ranges from 2 years to 16 years. The dispensary cases range in duration from 2 days to six months.

Ages of the private cases varied from 18 to 58 years. The dispensary cases varied from 5 to 50 years.

Most of the cases, especially the private ones, have undergone a gamut of treatment. They run from dietary restrictions, calcium injections, vitamin C administration, auto-hemotherapy, peptone extracts, arsenic, foreign proteins, acids and alkalies, laxatives, mineral waters, colonic enemas, etc. In fact all forms of known treatment have been given. For the acute symptoms, relief was afforded by the adrenalin and ephedrine

group of drugs. The patients reported that these forms of treatment have given them some temporary relief, but when they accidentally eat the offending foods, they develop the condition again. Those cases who are careful enough not to eat the offending foods complained that they lose much weight on account of the limitations of their diet. Like any human being, they are after a form of treatment that would make them enjoy all kinds of food that their lucky brethren eat. Upon being told that they could eat whatever food they liked during and after treatment, they were only too willing to submit themselves to the procedure.

NUMBER OF INJECTIONS

Among the private cases, the number of injections required to effect a "cure," varied from 5 to 25 injections, the average being 15. Among the dispensary cases, the number of injections varied from 1 to 18, the average being 5.

One of the earliest effects noted during treatment was the disappearance of the pruritus, which was felt usually at the second or third injection, the presence of the wheals notwithstanding. The latter usually required more injections than was necessary to make the pruritus disappear.

RESULTS OF TREATMENT

All the patients who underwent our prescribed course were "cured" in the sense that subsequent taking in of foods which they have observed to have always brought on the attacks no longer evoked an urticarial reaction. A complete follow-up of the private cases from six months to almost five years indicated no further recurrence. Among the dispensary cases, no complete follow-up is possible. The fact that the cases did not return altho they were told to return in the event of a reaction, may suggest that these cases, like the private cases, were also cured. The remarkable observation with the procedure is the absence of the urticarial reaction after the ingestion of certain foods which before treatment always caused a reaction. This was taken as the criterion of cure.

UNTOWARD REACTIONS AND COMPLICATIONS

There are a few untoward reactions observed in a few patients. They are, however, not annoying enough to merit discontinuance of the treatment.

An immediate feeling of weakness that passes off in a few minutes was observed in some cases. Some complained of mild headache, six hours after injection and lasting for about two hours. Others had a slight rise of temperature usually accompanied by malaise and insomnia. Loss of appetite during treatment was complained of by a few.

The local reactions were pain at the site of injection which last from six to twelve hours. In three cases there was abscess formation which was incised and drained.

In one case of Quincke's edema, the injection caused the flaring up of symptoms so much so that the patient did not continue treatment. She is the only one in the series who did not continue treatment.

REVIEW OF LITERATURE

A review of literature revealed that the procedure was first employed by Jausion and Paleologue in 1929. They tried the procedure in all allergic cases. They tried it on the same principle for which Sicard was employing auto-hemotherapy. Considering that the urine is a "cemetery of molecules," they believe that better results could be obtained by urine instead of blood.

Jausion, in collaboration with Giard and Martinaud [1] published in 1933 their employment of auto-urotherapy in 456 cases of different allergic conditions. Of these, 342 were cured, 75 obtained improvement, and 39 did not improve at all.

Matusevich and A. Bergman [2] employed the method in spasmodic rhinitis, considering the condition as an allergic reaction. Dancenis [3] used the procedure in eczema and asthma. Johnston,[4] Krebs [5] Jausion,[6] Risquez,[7] and Herz [8] employed it in different allergic conditions.

COMMENTS AND CONCLUSIONS

The acid test of any treatment is time and number of cases. Our cases are too few to enable us to draw a satisfactory con-

clusion. The fact, however, that our cases, for clinical purposes, were cured may warrant the suggestion that auto-urotherapy has a definite place in the management of urticaria.

Forty-one cases in all have been treated by the method and all responded well.

The technic of the method is simple, the treatment is cheap, and the results so encouraging as to merit further trials and observation.

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MEASUREMENT OF CIRCULATION TIME WITH LOBELINE *

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Circulation time is defined as the time necessary for the blood to traverse a given distance in the vascular system, it is therefore a measure of the velocity of the blood. Circulation time is influenced by many factors. It varies inversely as the velocity of the blood and cardiac output. In health, the circulation time and the blood volume are so adjusted that one influences or is influenced by the other. Blood viscosity, temperature, pulse rate, cross section of the vascular tree, metabolic rate, etc. also affect it. Because of the fact however that the circulation time is definitely slower in a few conditions, the most important of which is heart failure, its determination has been found useful in the diagnosis and prognosis of this condition. According to Tarr,[1] "the condition of greatest clinical importance in which a slowing of the blood stream occurs is congestive heart failure. Here it is independent of the etiological factor, whether rheumatism, hypertension, arteriosclerosis or syphilis." It has been used to differentiate between the fluid accumulations due to heart failure and those due to nephritis, liver disease or new growth. In the same article, Tarr mentions that he found a prolonged circulation time in every patient with edema of cardiac origin so consistently that he suggests that "a normal circulation time in the presence of undoubted clinical cardiac failure should make one search for factors which would tend to increase the velocity of blood flow, the most usual of which are hyperthyroidism, fever and severe anemia." It has also been utilized to detect impending decompensation in the absence of the more common symptoms, some workers having found a definite slowing even before the venous pressure and the vital capacity were significantly altered. In cardiac asthma, circulation time is prolonged, in bronchial asthma it is normal. Dyspnea and cyanosis due to emphysema or other intra-pulmo-

* Read at the 38th Annual Convention, Philippine Medical Association, April 25, 1940.

nary condition can be differentiated from those due to heart failure. In some cases of congenital heart defect, determination of the circulation time may be of diagnostic value. It can be used to follow the progress of digitalis therapy along with the electrocardiogram. Soma Weiss [2] found that the circulation time in heart failure due to beriberi is normal or faster, in all other cases of heart failure it is slower. If this is verified here, it will mean a contribution of incalculable importance, for the diagnosis of beriberi is often made only with the greatest difficulty. Finally, circulation time has been used, though with less frequency, in a group of miscellaneous conditions among which are hyperthyroidism (short C. T.), myxedema (long C. T.), dehydration, polycythemia, etc.

Various methods have been devised to measure circulation time, the most important of which are those of Blumgart and Yens, who used a radioactive substance [3]; Weiss, Robb and Blumgart, who used histamine [4]; Tarr, Oppenheimer and Sager, who used decholin [1]; Robb and Weiss, who used sodium cyanide [5]; Goldberg, who used calcium gluconate [6]; Kvale and Allen, who used a mixture containing magnesium sulfate, calcium gluconate, sodium chloride and copper sulfate [7]; Fishberg, Hitzig and King, who used saccharin.[8]

From a study of these various methods it has generally been decided that the ideal substance for measuring circulation time should have the following qualities:

1. It should be non-toxic in the dose employed.
2. It should not influence the phenomenon under study.
3. It should be rapidly eliminated or detoxified.
4. The end reaction must be objective and readily discernible or recordable.

Considered from these points of view therefore, almost all of the pharmacologic methods enumerated above are deficient in that the end result they produce is subjective. The investigator has to depend on the patient to indicate the end reaction, a sweet taste in the case of saccharin, a bitter taste in the case of decholin, a hot sensation in the case of calcium. Histamine and cyanide, although they give an objective end point, have reactions that may be disagreeable. For example, in the histamine method, headache usually follows the use of the drug, and with cyanide,

intense dyspnea, labored breathing and tachycardia result from the larger doses [5].

Recently lobeline was used by the Russian authors Teplov and Sor and the work was repeated in America by Berliner [9] and Piccione and Boyd.[10] Interest was created by the fact that this substance as used in the measurement of the circulation time gave an objective end point, a cough, and therefore, theoretically at least, overcomes one of the objections to the use of drugs in the measurement of blood velocity. This study therefore was undertaken with the following ends in view:

1. To test the efficiency of lobeline in the measurement of circulation time.
2. To obtain normal values for Filipinos.

Some of the questions to which we sought an answer were the following:

1. Is lobeline safe to use under local conditions?
2. What are the untoward reactions?
3. What is the optimum dose for Filipinos?
4. What factors determine the dose?
5. What preparations of the patient are necessary?

Material and Procedure

The test was performed on patients in the medical and surgical wards of the Philippine General Hospital. The cases were divided into two groups. The first group comprised individuals in whom cardiovascular, renal or blood disease could be excluded by the history, physical examination and laboratory procedures. The second group was composed of patients who had fluid accumulations in the thoracic cavity, abdomen or extremities, or who were suffering from diseases which would affect the velocity of the blood.

The determinations were made at least three hours after breakfast. The patients rested on bed at least one half hour before the injection was made. The drug * was injected into the antecubital vein, with the patient lying down. Before the injection was made, the tourniquet was released and a period of 30 seconds was allowed to pass before the drug was introduced

* We are grateful to Inhelder, Inc. who kindly furnished us with ampules of "Lobeline, Sandoz".

into the vein. The injection was made rapidly, the whole quantity being given in not more than 3 seconds. The time between the start of the injection and the appearance of the end point was taken as the circulation time.

Results and Discussion

In general our findings give a circulation time for Filipinos which is not very different from that found by other workers. Thus our first group, which for the purpose of this paper was considered as normal, gave an average circulation time of 10.0 seconds. The highest was 13.5 and the lowest 6.5 seconds. Berliner obtained a normal circulation time of 8.5 seconds, Teplov and Sor 13.4, Stanojevic 10.3 and Piccione and Boyd 11 seconds.

Having obtained this figure we next proceeded to determine the circulation time in a variety of conditions. Marked slowing was noted in all cases of cardiac decompensation. The longest circulation time we obtained was 46 seconds and the shortest 20.5 seconds.

In no case of fluid accumulation due to causes other than heart failure was there any slowing of circulation time. It was surprising to see how patients with markedly distended abdomens due to ascites or with fluid oozing from the skin from huge accumulations of fluid in the subcutaneous tissues nevertheless gave a normal circulation time. This is in sharp contrast to those who had a minimal edema of the extremities due to cardiac lesion but who had their circulation time prolonged five or six times above normal.

The procedure did not give any untoward reaction or even distressing symptom in 100 cases. The end point we took was the cough; this varied from a slight cough or two as if the patient were clearing his throat, to a series of coughs coming one after the other and lasting for about 20 seconds. Only one patient complained of nausea after a somewhat prolonged series of coughs, but the feeling passed off in three minutes leaving no after effect. The end point usually starts with a facial contortion on the part of the patient. He screws his lips together, shuts his eyes and turns his face uneasily from side to side and then coughs. The initial cough may disappear without any further manifestation or it may usher in

a short paroxysm of coughs which disappears as suddenly as it comes. Within five minutes all signs of the reaction have disappeared and the test can be repeated. Asked what they felt, the patients described most commonly two sensations. Some mentioned a burning or irritating sensation in the throat. Others described a choking feeling as if there were smoke in the throat which had to be expelled. All were agreed that as soon as one had coughed the oppression was relieved.

With regards to the end point, it should be pointed out that one may take any stage of this reaction as the end. Berliner used the cough, Piccione and Boyd used the tickling sensation in the throat. In our experiments, we thought at first of timing the patient with the appearance of the facial contortion or the turning of the face from side to side. We were led to study this part of the reaction, because in some cases we did not elicit a cough although the grimace was present. On questioning, the patients admitted that they had felt like coughing but had suppressed the desire. However, this grimace was not always present, some patients coughed without any preliminary motion of the head or change of expression.

With regards to the dose, we found out that this could not be calculated from the age, sex or weight of the patient. One individual will inexplicably not be affected by the highest dose we have given, while another will give a violent reaction with the minimum dose. Age, sex and weight did not give a constant correlation. The intensity of the end reaction and the reaction itself seemed to depend on the speed of the injection more than on any other factor. Thus 5 milligrams, the highest dose we have given, if injected over a period of more than five seconds often gave no result, while 3 mg. if introduced within 3 seconds may give a marked end point. In general 3 mg. sufficed for most of our cases. This dose was enough to produce a discernible cough in the majority of cases. Those that did not were tested again with 5 mg. and they always gave a satisfactory response. We have not had any occasion to use the 12 mg. which some workers have employed.

Mechanism of Action

Lobeline is an alkaloid of lobelia inflata supposedly possessing selective action on the respiratory center. Heyman et al [11],

think that the action is on the carotid sinus which is stimulated by the drug and in turn reflexly stimulates the respiratory or cough center. We tried to confirm this; we selected a group of patients and took thir pulse rate and blood pressure before and after administration of the drug. "The carotid sinus is a mechanism whereby both pressor and depressor effects are mediated. Electrical stimulation of the sinus wall causes marked slowing of the heart rate, vasodilatation and a fall in blood pressure [12]".

Our results are shown in the accompanying table. In only a few cases was the pulse rate slowed, in many it was actually increased. With regards to the blood pressure, in no case was there diminution, in most cases there was an increase of a few millimeters. This would tend to throw doubt on the statement that the drug stimulates the carotid sinus first; the possibility that it acts directly on the cough center must be considered.

Conclusions

1. Lobeline is a useful drug for the determination of the circulation time in the sense that it gives an objective end point.

2. The normal circulation time for Filipinos is not very different from the normal circulation time found in other people. In our case, under the conditions described above, it was 10.0 seconds.

3. The determination of the circulation time is a valuable diagnostic procedure the chief use of which is the differentiation between cardiac edema on one hand and renal, hepatic or other edema on the other hand.

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TABLE I.—*Circulation Time Measurements on Patients Without Evident Cardiovascular, Renal, or Blood Disease*

No.	Patient's Initials	Sex	Age	Diagnosis	Temp. Cent.	Pulse Rate before inj.	Pulse Rate after inj.	B. P. mm. Hg before	B. P. mm. Hg after	Circulation Time (Secs.)	Remarks
1	A. T.	M.	35	Pleurisy with effusion, recovered	36.9°	64	70	104/70	104/70	6.5	
2	P. P.	F.		Arthritis, knee jt., left, syphilitic (improved)	37.0°	78	80	100/60	104/70	7.0	
3	F. B.	M.	29	Gall bladder disease, chronic (improved)	37.0°	90	92	100/60	120/80	Failure 7.0	5 mg. Lobeline 5 mg. Lobeline
4	N. V.	M.	38	Peptic ulcer, chr. (improved)	36.8°	80	80	100/60	108/64	7.5	
5	F. M.	M.	24	Peptic ulcer, chr. (improved)	37.0°	54	60	114/60	124/80	7.5	
6	O. G.	M.	23	Fracture, tibia, malunited	37.2°	86	86	100/60	120/70	7.5	
7	G. M.	M.	27	Gall bladder disease, chronic (improved)	36.9°	68	70	80/50	94/70	8.5	
8	M. S.	M.	45	Polyarthritis, rheu., recovered	—	96	92	—	—	9.0	
9	D. T.	M.	25	Peptic ulcer, chr. (improved)	—	88	80	—	—	9.0	
10	M. C.	F.	34	Gall bladder disease, chronic (improved)	37.1°	88	82	130/80	136/90	9.0	
11	L. A.	M.	30	Monoplegia cruralis, left, old, post poliomyelitis	37.0°	68	62	108/70	120/80	9.0	
12	T. G.	M.	31	Lobar, pneumonia, recovered	37.1°	84	90	114/70	128/70	9.5	
13	M. L.	M.	44	Gall bladder disease, improved	37.0°	60	64	110/60	118/70	9.5	
14	V. D.	F.		Nephrolithiasis	—	—	—	—	—	9.8	
15	C. D.	M.	31	Arthritis deformans	36.8°	80	72	114/64	110/62	10.0	
16	D. M.	M.	26	Appendicitis, chronic	36.9°	62	62	108/60	112/68	10.0	Severe paroxysm
17	P. R.	M.	39	Peptic, ulcer, chr., improved	37.0°	56	54	140/80	150/90	10.0	
18	V. H.	M.	28	Arthritis, syphilitic, recovering	37.0°	80	88	96/50	100/60	10.0	
19	C. I.	M.	16	Pneumonia lobar, recovered	36.9°	74	72	110/70	118/70	10.0	
20	L. T.			Poisoning. HCl suicidal, recovered	37.0°	76	80	98/50	110/80	10.0	
21	N. R.	M.	16	Polyarthritis, syphilitic recovering	—	—	—	—	—	10.5	

TABLE I.—Continued

No.	Patient's Initials	Sex	Age	Diagnosis	Temp. Cent.	Pulse Rate before inj.	Pulse Rate after inj.	B. P. mm. Hg before	B. P. mm. Hg after	Circulation Time (Secs.)	Remarks
22	R. O.	M.	21	Peripheral neuritis, B, paralytic	37.0°	78	78	110/70	114/70	10.5	
23	S. L.	F.	—	Peripheral neuritis, B, paralytic	—	—	—	—	—	10.5	
24	P. B.	M.	39	Amebiasis, chronic	36.7°	86	72	128/80	130/80	10.5	
25	R. G.	M.	15	Fracture, simple, tibia, left	37.0°	78	74	116/62	120/60	11.0	
26	G. L.	M.	60	Peptic, ulcer, chr., improved	36.8°	64	74	110/70	120/70	11.5	
27	B. S.	M.	38	Gall bladder disease, chronic, improved	37.1°	82	68	120/80	124/80	12.0	
28	M. R.	F.	—	Peptic ulcer, chronic, improved	—	—	—	—	—	12.5	
29	M. L.	M.	23	Peptic ulcer, chronic, improved	37.1°	84	68	108/60	114/70	12.5	
30	M. M.	M.	64	Peptic ulcer, chronic, improved	36.8°	72	72	104/64	104/60	12.5	
31	F. D.	M.	42	Arthritis, chronic, gonorrheal	36.8°	72	72	104/64	104/60	12.5	
32	T. G.	F.	41	Rheumatic arthritis	37.0°	70	66	118/68	124/80	13.0	
33	J. S.	M.	58	Influenza, recovered	36.8°	88	84	124/70	126/70	13.0	
34	T. M.	M.	—	Peripheral neuritis, B	—	—	—	—	—	13.5	

EFFECTS OF HIGH DOSES OF NICOTINIC ACID ON HUMAN EPIDERMOID CARCINOMA

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Nicotinic acid, the so-called pellagra-preventive or P-P factor, is a vitamin successfully used in the treatment of pellagra (Fouts, Helmer, Lepkovsky and Jukes,[1] Spies,[2] Smith, Ruffin and Smith [3]). It has also been found effective in radiation sickness (Spies et al [4], Graham [5]), sprue (Fuchs and Wisselinck [6]), delirium tremens (Mainzer and Krause [7]), anemia of the prematurely born (Goebell [8]), xerostomia (Saphir [10]), Vincent's disease (King [11]) and non-infectious summer diarrhea (Teasley [12]).

The mode of action of nicotinic acid in the treatment of pellagra and the other above-mentioned diseases has not been definitely determined but it is assumed that the mechanism is based on the fact that nicotinic acid, being the most essential constituent of the respiratory catalyst, "codehydrase," its administration may increase this catalyst. That such a transformation of nicotinic acid into codehydrase occurs within the human body was proven by Kohn et al [13]. These workers showed that the ingestion of nicotinic acid caused an increase of the so-called V-factor—a substance promoting the growth of some bacteria and probably identical with codehydrase.

Warburg was the first to show an anomaly in the gas metabolism of malignant tissue [14, 15, 16]. He and his co-workers found that the oxygen consumption of tumor tissue was smaller than that of normal tissue, and particularly, that the depressive effect of oxygen intake on lactic acid formation, known as the Pasteur-Meyerhof reaction, was very much diminished in malignant tissue. This phenomenon constitutes the so-called anaerobic glycolysis of tumor tissue. In experiments performed by Frisch and Willheim [17, 18, 19] and Wetzler-Ligety and Willheim [20, 21], there were indications that the fraction obtained from tumor tissue by boiling out with water was somehow

altered as compared with a similar fraction from normal tissue. This extract obtained from tumor tissue had a reducing power which interfered with the course of oxidizing reactions. The authors could show that the production of lactic acid by muscle extracts, when stopped by the oxidizing functions of added quinone, reappeared upon the addition of these tumor tissue extracts. This phenomenon was not observed upon the addition of *normal* tissue extracts. These results seem to offer an explanation for the mechanism of the characteristic anaerobic glycolysis of the tumor tissue. It was also inferred that the substances responsible for this behaviour of the tumor extracts belong to the co-ferments of tissue respiration. The co-ferments, therefore, were thought to be characteristically altered in tumor tissue. Von Euler and his co-workers [22, 23] also found that the codehydrase of tumor tissue really differs from that of normal tissue by being mostly in the reduced state. It is, therefore, plausible that an increased administration of nicotinic acid may normalize, at least partly and temporarily, the altered respiratory apparatus of tumor tissue.

This possibility and the established curative action of nicotinic acid on pellagra and its accompanying skin lesions spurred us to study the influence of high doses of nicotinic acid on human tumor growth in general, and on epidermoid carcinoma in particular.

For this study we have particularly chosen cases of epidermoid carcinoma of the mouth cavity because these newgrowths, which are frequently seen in the local tumor clinic, are easily observed and controlled by repeated biopsies. We administered to the patients nicotinic acid in tablets in doses up to 900 milligrams daily. In some cases we tried to support the nicotinic acid treatment with 600 milligrams daily of methylene blue in capsules. Methylene blue was added because it is well known as an oxygen carrier in biological experiments (Thunberg [24]) and had already been used as such in the treatment of poisoning with prussic acid and carbon monoxide (Geiger and Gray [25]).

We shall describe in this paper first, the results of the repeated biopsies, and then the clinical condition of the patients before and after the treatment.

The microscopic changes observed up to the present are the most interesting because they are the most constant. We

noted that typical epidermoid carcinomas, consisting mainly of abundant, slightly differentiated and deeply stained cells and only scanty keratin pearls, were altered by a markedly increased keratinization. After some weeks of nicotinic acid treatment the degree of kerato-hyalinization was in some cases so striking that the character of the microscopic picture was completely changed. We saw in some instances a considerable number of well-developed keratin pearls and in others large cords of kerato-hyalinized tissue not present in such a degree before the treatment. The tumor cells themselves lost a great part of their ability to be stained. We are inclined to consider these changes as a highly increased differentiation which might be the consequence of a primarily retarded growth. This retardation of growth afforded more time for the cells to differentiate, whenever they were capable of such differentiation because of their histogenesis. These histological findings apparently occur chiefly in epidermoid carcinoma because it is capable of differentiation into keratinized epithelium.

The second striking change we often noted in our histological preparations was much leukocytic infiltration, mostly surrounding the keratinized areas. It is of course impossible to state up to now whether or not the inflammatory appearances were secondary to the kerato-hyalinization. The accompanying pictures illustrate the changes reported above.

Clinically the changes in the gross appearance of the newgrowth and the general condition of the patient during the nicotinic acid treatment were not as uniform as those in the histopathological studies. The first observation in most patients with epidermoid carcinoma was a cleansing of the tumor surface because of the pushing off and shedding of the superficial necrotic coats. In ulcerative processes this was usually accompanied by a drying up of the surface, occasionally followed by epithelization. In cauliflower newgrowths we observed two interesting phenomena: first, the appearance of numerous, often confluent, whitish lines and spots apparently caused by kerato-hyalinization; and, second, occasionally the formation of deep fissures at the edge of the newgrowth.

But these phenomena which were apparently favorable for the patients occurred only in superficial lesions. When the tumor deeply infiltrated the surrounding tissues, the clinical pic-

ture was overshadowed by a strong inflammatory reaction involving the whole area affected by the newgrowth. A consequence of this inflammation on several occasions was the appearance of much secretion from the tumor surface. Similar inflammatory phenomena were observed very often in metastatic lymph nodes.

The most important question that arises now is the influence of the above-mentioned changes on the further growth of the tumor. This question can not be answered definitely. We can only state that we had several patients in whom a visible cessation of growth was effected. In a few patients, even a diminution in size could be observed. It is true that our time of observation was only a year at most, but the patients considered in this paper were easily observed and the newgrowths had appeared and developed in a relatively short time before the beginning of the treatment.

Up to now the best clinical results corresponding to the reported histopathological findings have been obtained in two types of newgrowths. The first type was the simple cauliflower tumor which had not yet infiltrated deeper layers and whose histological structure revealed from the start a tendency to differentiation. Out of 21 cauliflower tumors of the mouth cavity observed in the past year, 12 were of this type, 9 of which presented a remarkable cessation of growth and even regression in size of the lesion after treatment through several months up to a year with nicotinic acid alone or combined with methylene blue. The second type of tumor which responded favorably was the superficial ulcerative process. In 4 patients who came to the clinic with such a process there were observed drying up, scabbing and epithelization of the ulcer which in 3 cases resembled actual healing.

In most of the patients treated, the general condition was markedly improved with subsidence of pains. Better sleep and greater appetite were spontaneously reported.

A large percentage of the patients that came to the tumor clinic were already affected with advanced, deeply infiltrating and metastasizing newgrowths. The effect of nicotinic acid on these patients was quite different from the others presenting superficial lesions. A few days after the beginning of the administration of nicotinic acid, inflammatory changes and ac-

companying pains appeared and dominated the clinical picture. Very often with time, suppurative processes, such as abscesses and fistulas, developed. Our study is not extensive enough for us to predict the further course of these advanced cases under nicotinic acid treatment. We have seen a few cases in which after treatment for months, large portions of the tumor were removed by suppuration and a certain clinical improvement was achieved but, of course, with formation of extensive tissue defects. At this stage we can not yet indicate whether this effect may be expected in a larger percentage of patients.

As to the influence of nicotinic acid on metastatic newgrowths our experience thus far does not warrant a definite conclusion. We have seen regional metastatic lymph nodes stabilized as to their growth and even diminish in size. On the other hand, there were other metastatic lymph nodes that became suppurative during the treatment. Two patients with liver metastases observed through a short time did not show any improvement. In this connection it is to be pointed out that the histological structure of not only the primary tumor but also of the surrounding tissue seem to affect the response of the patient to this treatment in the sense that mainly epidermal tissue acquires an anti-cancerigenic property under the influence of nicotinic acid. Perhaps this runs parallel with the anti-pellagric action of nicotinic acid.

Regarding other types of newgrowth, a favorable response such as that obtained in patients with epidermoid carcinoma was hardly to be expected. Still we observed some patients with a marked retardation of growth which was non-epidermoid carcinoma. But unlike the tumors in the human buccal cavity which are easily observed and controlled by repeated biopsies, the newgrowths of internal organs exclude, of course, any reliable examination. Perhaps animal experiments might be of some value here.

For the present we shall restrict our conclusions to epidermoid carcinoma of the skin and mucous membrane. But we must emphasize that a new cure for malignant tumors is not claimed in this paper. We consider all the phenomena observed by us to be interesting, mainly as a new effect of nicotinic acid, suggesting that the realm of its biological actions is not yet fully explored and, therefore, calls for further research. Whether

the above-described influence of high doses of nicotinic acid on cancer tissue will ever have a definite practical value, only a longer experience on more varied material can tell.

SUMMARY

1. Based upon the anomalies of the respiration and glycolysis of tumor tissue (Warburg et al) and the probable participation of the respiratory co-ferments in these disturbances (Willheim and co-workers; v. Euler and co-workers), a study of the influence of high doses of nicotinic acid,* sometimes combined with methylene blue, on human epidermoid carcinoma, especially of the mouth cavity, was made by the authors.

2. Histological changes: An increase of keratohyalinization of the cancerous tissue took place to such a degree as to considerably change the histological structure. Furthermore, an increased inflammatory infiltration was observed.

3. Macroscopic changes: Cauliflower newgrowths presented marked cessation of growth, demarcation from the surrounding normal tissue, whitish spots, and sometimes even a diminution in size. Drying up, scabbing and epithelization were observed in superficial ulcerative processes. Deeply infiltrating newgrowths responded as a rule with strong inflammatory reactions.

4. Clinical observations: Cauliflower and superficial ulcerative processes seem to be very often favorably influenced.

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* Our thanks are due to the Manila branch of the Abbott Laboratories for the supply of nicotinic acid tablets.

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ILLUSTRATIONS

Fig. 1. H.F.—Epithelioma, inner cheek, right.

A.—(× 170) At the beginning of the treatment.
B.—(× 680) At the beginning of the treatment.
C.—(× 170) After two months treatment.
D.—(× 680) After two months treatment.

Note the increased keratinization.

Fig. 2. C.K.—Epithelioma, tongue, edge, posterior third, left.

A.—(× 170) At the beginning of the treatment.
B.—(× 680) At the beginning of the treatment.
C.—(× 170) After two weeks treatment.
D.—(× 680) After two weeks treatment.

Note beginning keratinization.

Fig. 3. R.L.—Epithelioma, inner cheek, left.

A.—(× 170) At the beginning of the treatment.
B.—(× 170) After two months treatment.

Note the increased keratinization and the decreased cellular affinity for stains.

Fig. 4. M.G.—Epithelioma, hard palate.

A.—(× 170) At the beginning of the treatment.
B.—(× 170) After two months treatment.

Note evidences of keratinization and inflammation.

FIG. 1-A

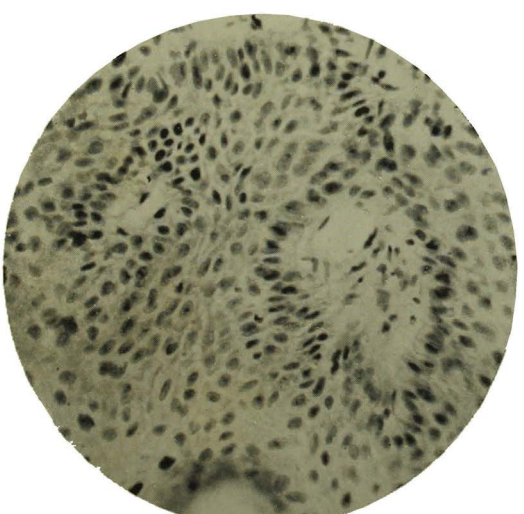

FIG. 1-B

FIG. 1-C

FIG. 1-D

FIG. 2-A

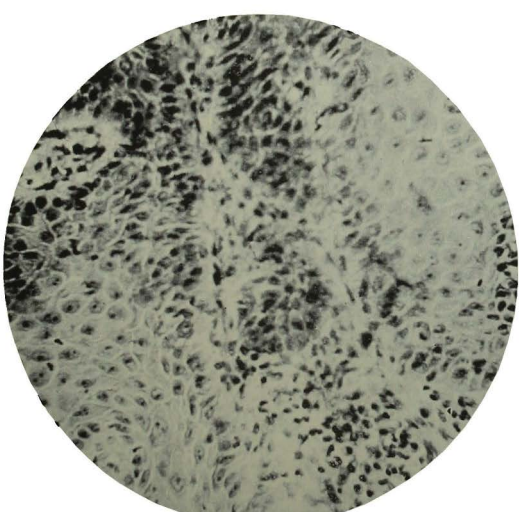

FIG. 2-B

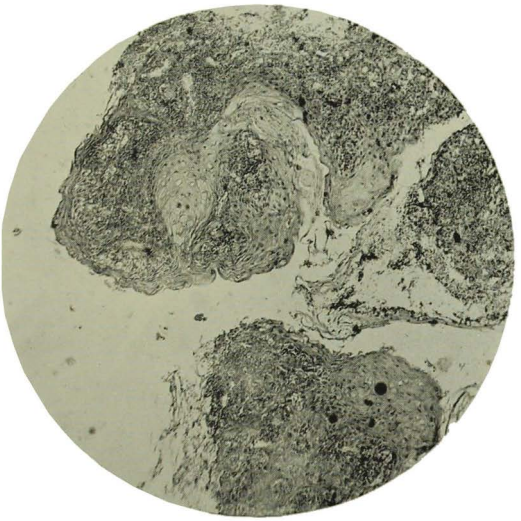

FIG. 2-C

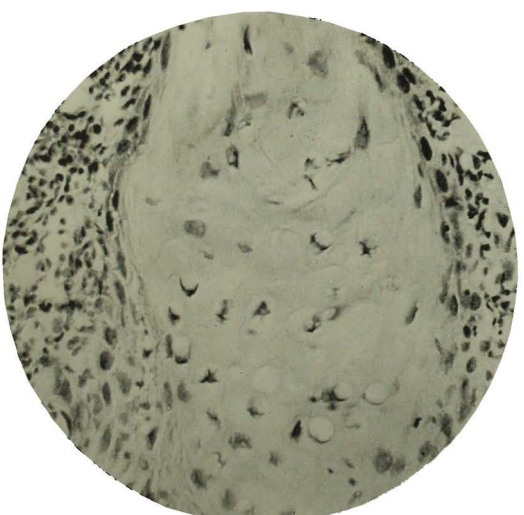

FIG. 2-D

FIG. 3-A

FIG. 3-B

FIG. 4-A

FIG. 4-B

THE BLOOD OF FILIPINO CHILDREN

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This paper is a continuation of "the Blood of the Newborn" by Stransky and Pecache.[7] The first part of this study deals with the hemoglobin content and the second with the differential blood picture of children from 2 to 16 years or more. The first two years of age are characterized by the frequent occurrence of anemias, low hemoglobin values even in healthy children, and last but not least by the lability of the hematopoietic apparatus on account of its constitution and frequent infections. We shall therefore discuss the blood of Filipino children in the first two years in another paper.

The hemoglobin level in children varies according to different authors. The survey of Nadolny and Weinberg[4] shows the following:

Ages	Perlin	Leichtenstein	Wiel	Widowitz	Stierlin	Carstanjen
1-2 years	78%	74-78%	—	62-110%	44-78%	70%
2-3 "	80%	75%	—	62-110%	44.78%	76%
3-4 "	80%	77%	83-110%	98%	44-78%	75%
4-5 "	84%	77%	83-110%	92%	44-78%	75%
5-6 "	84%	79%	—	86-110%	80.5%	75%
6-7 "	85%	80%	—	86-110%	80.5%	65%
7-8 "	85%	80%	—	86-110%	80.5%	85%
8-9 "	85%	79%	—	86-110%	80.5%	73%
9-10 "	85%	79%	—	90-110%	80.5%	70%

These differences are probably due to the different methods used because 100% hemoglobin is equivalent to 13-18.5 gm. hemoglobin per 100 gm. of blood depending upon the different hemoglobinometers used. Therefore Perlin[5] gives not only the hemoglobin percentage but also the value in grams.

Ages	Number of Cases	Hemoglobin %	Gr.	Red Cell Ct.	W. Cell Ct.
2 years	13	71.5	11.83	4,997,000	11,217
3 "	7	72.5	12.00	5,059,000	9,875
4 "	13	75.5	12.44	5,118,000	11,010
5 "	16	77.5	12.90	5,189,000	9,813
6-10 "	7	78.0	13.00	5,042,800	8,355
10-15 "	9	81.00	13.49	5,196,450	8,555

The fluctuations are well seen in the following table:

AGES	Hemoglobin Min. %	Grs.	Max. %	Grs.	Red Cell Count Min. Millions	Max. Millions	White Cell Count Min. Thousands	Max. Thousands
2 years	58	9.66	78	13.00	4.75	5.6	8.24	13.4
3 years	60	10.00	80	13.32	4.9	5.35	8.9	11.6
4 years	70	11.66	84	14.00	4.0	5.5	8.6	13.4
5 years	72	12.00	81	13.49	4.7	5.6	8.8	11.2
6-10 years	74	12.39	84	14.16	4.2	6.0	7.8	9.22
11-15 years	78	13.00	88	14.66	4.8	6.0	7.8	8.9

It is easily seen that the fluctuations are very marked in the hemoglobin values and red cell counts. This fluctuation is also found in the survey of Nadolny and Weinberg [4] on the white cell counts.

Ages	Karnitzky	Rabinowitsch	Perlin
	9,400	6,500	
1-2 years	6,900-13,100	4,800-8,400	8,800-15,000
	9,400	7,350	
2-3 years	6,900-13,100	5,000-9,200	8,200-13,400
	9,400	6,400	
3-4 years	6,900-13,100	4,200-9,300	8,900-11,600
	9,400	6,560	
4-5 years	6,900-13,100	4,800-8,400	8,100-13,400
	9,400	6,100	
5-6 years	6,900-13,100	5,200-8,600	8,800-11,200
	7,900	6,800	
6-7 years	5,440-12,400	5,200-9,200	7,800-9,200
	7,900	6,350	
7-8 years	5,440-12,400	4,800-8,800	7,800-9,200
	7,900	6,440	
8-9 years	5,400-12,400	4,200-8,200	7,800-9,200
	7,900	6,160	
9-10 years	5,440-12,400	4,200-10,200	7,800-9,200

While there are no marked differences in the leucocyte counts of the different ages, yet there is a tendency to decrease with the progredient ages. A short survey of the differential

blood picture (before the hemogram era) of Schloss is given below.

Ages		Neutrophiles %	Lymphocytes %	Monocytes %	Eosinophiles %	Basophiles %
	Maximum	39.7	58.8	11.7	6.0	0.5
1-2 yrs.	Minimum	27.6	45.3	6.7	1.6	0.0
	Average	36.3	51.2	8.5	3.2	0.2
	Maximum	44.3	55.0	11.3	6.0	1.2
2-3 yrs.	Minimum	33.2	43.5	5.0	0.5	0.0
	Average	38.7	49.0	8.2	3.1	0.4
	Maximum	54.1	47.6	16.2	4.2	0.9
3-4 yrs.	Minimum	36.2	32.2	5.0	1.5	0.0
	Average	44.7	39.1	11.2	2.8	0.5
	Maximum	51.7	49.5	6.7	4.0	0.6
4-5 yrs.	Minimum	42.2	38.4	3.4	1.6	0.3
	Average	48.5	42.1	6.0	2.6	0.3
	Maximum	61.8	36.7	16.0	4.7	1.0
5-6 yrs.	Minimum	52.6	21.2	6.5	5.7	0.3
	Average	56.5	29.9	10.0	2.5	0.6
	Maximum	61.3	34.1	15.7	4.7	0.6
6-7 yrs.	Minimum	52.3	24.5	8.1	0.1	0.0
	Average	56.0	30.4	10.8	2.2	0.2
	Maximum	72.0	39.1	15.2	3.5	0.2
7-8 yrs.	Minimum	45.2	21.1	6.7	0.0	0.20
	Average	54.4	32.5	11.6	1.6	0.1
	Maximum	66.0	38.2	16.3	2.6	0.6
8-9 yrs.	Minimum	47.2	25.0	4.5	2.0	0.0
	Average	56.4	31.0	9.8	2.3	0.3
	Maximum	64.2	36.1	9.6	4.3	1.3
9-10 yrs.	Minimum	53.2	18.1	6.0	1.5	0.1
	Average	60.4	28.9	6.9	2.9	0.5
	Maximum	69.5	35.2	8.5	3.5	0.7
10-11 yrs.	Minimum	54.4	20.5	6.5	1.0	0.0
	Average	61.7	28.1	7.4	2.2	0.3
	Maximum	67.0	30.2	8.3	4.0	0.5
11-12 yrs.	Minimum	56.5	23.2	7.1	1.2	0.0
	Average	61.8	27.7	7.3	2.5	0.2

We gave these tables in order to compare our values among Filipino children with those found by Schloss [6] in U. S. A. Because of the hemogram, we would like to emphasize that according to Zibordi, there is no marked change in the ratio of the stab to the segmented cells in the different ages.

Considering the different reports in literature we must agree with Washburn [9] that in healthy children, the leucocyte count may vary in the same child from 5,000 to 24,000 even in the absence of a demonstrable disease. In eighty percent of the cases, however, the count is between 8,000 to 16,500. The differential blood picture also fluctuates. The lymphocytes are more or less constant but the neutrophiles vary from 5 to 63%, all the granulocytes from 10 to 68% and monocytes from 1 to 18%. According to Kato,[3] there are more lymphocytes than granulocytes in the first years of life until the fourth year when these two types of cells become equal in number. After the fifth year, the lymphocytes steadily decrease until the fifteenth year when their number is but one half the granulocytes.

Our observations were made on the children of Welfareville. We used the "Sicca" method described in the paper of Stransky and Pecache in the hemoglobin determination. We went to Welfareville twice a week, took the blood of eleven children at a time and made the examinations in the Philippine General Hospital. On account of technical difficulties, the red and white counts were not made. At the same time we dispensed with these latter examinations because we know that the average red cell count does not vary much in the different periods of life and in case of the average white cells there are even less changes although the count may vary in the same individual.

We wish to state that the children in Welfareville are well nourished with better living conditions than most of the poor Filipino children. This is probably why their hemoglobin values are higher than those of the children of poor families. The differential blood picture is, however, the same in all the children. We hope to complete our studies in the future by examining the school children in the different districts of Manila.

Probably this is the first study establishing these different blood values among apparently normal Filipino children. We can thus compare the blood of ill and healthy children and thereby study the blood changes produced by different diseases.

The Schilling hemogram which has been described in detail by Stransky in the No. 4, vol. 1 issue of the Acta Medica Philippina was used for the differential counts.

Our cases are divided into male and female groups. Each group is further subdivided into age groups. Two tables were made to show the main values in males and females and after this another table was prepared showing the maximum and minimum fluctuations and the average values for both sexes. The yearly grouping in boys is made from 2 to 16 years and all the cases above 16 years are included under one group while the yearly grouping in females is from 2 to 15 years and the older cases are included under another group. We only have two males and two females under two years of age. The whole material comprised 260 males and 181 females. Their age distribution is not uniform but we cannot do otherwise than utilize the materials that are available. The averages shown in the last table is given by the averages of equal males and females.

As previously stated the hemoglobin values are very high. In the third year of life, however, they are still low. According to our experiences, the hemoglobin of Filipino children is very low at the end of the first year of life, then it gradually rises and reaches its highest level at 8-9 years. The low hemoglobin level in the first year of life is due to two factors, (1) nutritional and (2) infectious factors. The nutritional factor is caused by the prolonged milk feeding and the taking of foods that are very deficient in iron while the infectious factor is caused by all kinds of infections. With increase in age, the infection becomes less frequent and hence the lesser incidence of post infectious anemia as the child grows older. It is well known that the hemoglobin level is lowest at the age of three months and then it gradually rises. Our Filipino new-borns are born with a hemoglobin percentage of 139 but it goes down to 100% in a few days and then it drops to 70% or even lower.

There are many striking peculiarities in the differential counts of our cases that are quite different from those reported in literature for white children. We have cases without neutrophilia at the ages of 15 and 16 years and even in older ones. The blood of the Filipino adult has more lymphocytes than that of an American or European adult. In the first year of life, the blood of white children is characterized by lymphocytosis.

According to Schloss, the average percentage of lymphocytes in the second year of life is 51.2, in the third it is 49, in the fourth it is 39.1, in the fifth it is 42.1 and in the sixth it is 29.9. Kato claims equal numbers of neutrophiles and lymphocytes in the fourth year of life in U.S.A. and from the fifth year, there are more neutrophiles than lymphocytes. In Filipino children the lymphocyte is around 50% until the age of 7 years. Then it oscillates between 40 to 45% after this age but there is never a marked predominance of the neutrophiles. Whether this lymphocytosis is due to a racial, climatic or nutritional influences, cannot be decided. We tried to examine the blood of European children to compare them with the Filipino children but our cases are too few to enable us to draw a definite conclusion about this point just now.

The number of stab cells is almost constant. They are always present and vary very slightly. This observation is important because it shows the clinical value of increased stab cells (shift to the left). The juvenile cells are rare and if present, they are found among young children and indicate the persistence of a labile hematopoietic system. A further sign of this labile hematopoietic apparatus is the higher stab cell values (5.3, 4.35, and 3.9%), in the three youngest groups while in the subsequent groups it varies from 3 to 3.5%.

The high average value of the eosinophiles is very interesting. We are giving below a table showing the incidence of eosinophilia in the different ages.

EOSINOPHILIA IN DIFFERENT AGES

Ages	Males			Females		
	No. of Cases	Eosinophilia	Aneosinophilia	No. of Cases	Eosinophilia	Aneosinophilia
2-3 years	15	5	2	17	3	3
3-4 years	19	4	2	24	8	3
4-5 years	12	7	0	15	9	1
5-6 years	16	12	0	19	16	0
6-7 years	17	10	0	8	4	0
7-8 years	13	7	0	3	2	0
8-9 years	17	7	0	12	10	0
9-10 years	18	13	0	9	6	0
10-11 years	24	17	0	15	10	0
11-12 years	19	13	0	12	9	0
12-13 years	21	13	0	21	13	0
13-14 years	24	20	0	11	7	0

Ages	Males			Females		
	No. of Cases	Eosinophilia	Aneosinophilia	No. of Cases	Eosinophilia	Aneosinophilia
14-15 years	12	10	0	7	4	0
15-16 years	20	12	0	9	4	0
Over 16 years	13	8	0	9	4	0

In the first two groups, eosinophilia is rather rare and aneosinophilia is not exceptional. In the subsequent ages, eosinophilia is very frequent and aneosinophilia is no longer observed. Our highest eosinophile count is 33.6%. The eosinophilia is more frequently due to intestinal parasitism. Among our cases Ascaris and Trichiuris eggs are almost always found in the stools, and very occasionally Ancylostoma eggs. In younger children there are cases where the hymenolepsis nana is the cause of the eosinophilia. In some cases giving low eosinophile count there are, as far as stool examinations show, no parasitic infections. Allergic conditions, like hay fever, bronchial asthma, urticaria, and allergic eczema, are attended by eosinophilia. The occurrence of eosinophilia in intestinal parasitism is also due to allergy against the proteins of the worms. This explains why not all cases of intestinal parasitism is attended by eosinophilia. When eosinophilia is present in healthy children, it is almost always a sign of intestinal parasitic infection. The high percentage of eosinophiles among our cases is undoubtedly due to the high incidence of intestinal parasitism among the children examined. We believe that the incidence of eosinophilia due to intestinal parasitism is even higher among poorer children whose living conditions are worse than those of the children in Welfareville.

We did not find any anemia caused by the intestinal parasites among the children in Welfareville, in spite of the different reports in the literature claiming that anemia due to intestinal parasitism is not exceptional. Our findings point only to the absence of heavy intestinal parasitic infections among the cases studied. This fact is well accounted for by the medical care and the better living conditions of the children in Welfareville. We are almost sure that a higher incidence of eosinophilia, and even anemia, exists among the children of the poorer classes. Undoubtedly, eosinophilia is very frequent among Filipino children. By comparing the eosinophile percentage we found among

Filipino children with those found by Schloss in white children, one will easily see the striking differences.

The percentage of monocytes in our cases is markedly lower than in the white children. With the exception of the 2-3 years age group (5.15%), the monocytes vary from 3 to 4% only. The normal values given for white adults by all workers are 4 to 6%, but for children it is even higher. Stransky and Pecache found this low monocyte counts among Filipino new-borns. We have no explanation for this low monocyte percentage. On the contrary we claim that this is a characteristic feature of the blood of Filipino children and adults as well. A comparative hematologic study of the whites and Filipinos in the tropics may lend some light on these findings.

The last interesting feature of the Filipino blood is the frequent occurrence of plasma cells. Below is a table showing the incidence of plasma cells.

PLASMA CELLS IN FILIPINOS

Ages	Males			Females		
	No. of Cases	Present	Absent	No. of Cases	Present	Absent
2-3 years	15	12	3	17	11	6
3-4 years	19	15	4	24	18	6
4-5 years	12	9	3	15	13	2
5-6 years	16	9	7	19	10	5
6-7 years	17	9	8	8	7	1
7-8 years	13	3	10	3	3	0
8-9 years	17	6	11	12	3	9
9-10 years	18	5	13	9	5	4
10-11 years	24	2	22	15	7	7
11-12 years	19	6	13	12	5	7
12-13 years	21	5	16	21	8	13
13-14 years	24	10	14	11	6	5
14-15 years	12	4	8	7	4	3
15-16 years	20	7	13	9	2	7
Over 16 years	13	2	11			

The average plasma cell percentage is 1.15 in the third year of life, 0.8 in the fourth and 0.95 in the fifth. Then it gradually drops to 0.1%. In the first year of life these cells are almost always present in the blood but in the later ages they almost always disappear completely. Plasma cells are absent in the blood of normal European children. These cells are of lym-

phatic origin and their presence indicates an irritation of the lymphopoietic tissues by chronic or repeated infections. The presence of a large number of these cells in the blood of Filipino children signifies the frequent occurrence of repeated infections in their first years of life, manifest or subclinical.

The absence or presence of basophiles among Filipino and white children does not show any differeence. There is, however, an increasing number of basophiles as the age increases.

SUMMARY

1. A study of the blood of healthy Filipino children between the ages of 2 to 16 years and some older ones is presented. The study embodies the observation on 441 cases, 260 males and 181 females.

2. The hemoglobin value of Filipino children is relatively low in the third year of life but it gradually increases with the age and attains its highest at 8 to 9 years.

3. The hemogram of Filipino children is characterized by lymphocytosis of about 50% until the age of 7 years when it oscillates between 40 to 45% without any tendency for the neutrophiles to predominate.

4. The percentage of segmented cells is variable while that of the stab cells is more or less constant. The latter averages 5.3% in the third year, 4.35% in the fourth, 3.9% in the fifth, and in the older children it remains between 3 to 3.5%.

5. There is a high incidence of eosinophilia among Filipino children due to intestinal parasitism. From 2 to 4 years, the eosinophilia is present in less than 50% of the cases but in the later ages it is around 70% or even more. Aneosinophilia occasionally occurs in the first years but never in later ages.

6. There is a low monocyte percentage among Filipino children. Among white children 4 to 6% monocytes or more, is normal while among Filipino children the value above 5% is only observed in the third year of life. In older children it is below 4% or it may even be around 3% only.

7. Plasma cells are pathologic findings among the whites but normal among young Filipino children. The average value at 2-5 years is around 1%. Then it gradually drops to 0.1%. Plasmacytosis is normal among young children but exceptional

in older ones. Plasmacytosis is a sign of chronic or repeated infections.

8. The percentage and occurrence of basophiles among Filipino and white children are similar.

AVERAGE VALUES FOR MALES

	cases	%	B	E	M	J	St.	S	L	Mo.	Pl.
2-3 Yrs.	15	74	0.2	4.3	—	0.2	4.0	31.4	53.6	5:0	1.3
3-4 Yrs.	19	90	0.3	4.7	—	—	4.9	40.0	45.1	3.3	0.8
4-5 Yrs.	12	88	0.2	5.0	—	—	4.0	35.5	51.4	3.2	0.9
5-6 Yrs.	16	90	0.5	8.3	—	—	3.0	34.2	50.1	3.4	0.5
6-7 Yrs.	17	92	0.4	5.8	—	—	3.3	38.6	47.3	3.6	0.4
7-8 Yrs.	13	90	0.6	6.8	—	—	3.5	44.6	40.9	3.4	0.2
8-9 Yrs.	17	93	0.2	6.2	—	—	3.7	42.5	44.4	2.7	0.3
9-10 Yrs.	18	92	0.3	8.7	—	—	3.4	42.1	42.3	3.0	0.2
10-11 Yrs.	22	91	0.4	8.4	—	—	3.4	41.9	42.7	3.0	0.2
11-12 Yrs.	19	91	0.4	8.0	—	—	3.6	44.0	40.6	3.2	0.2
12-13 Yrs.	21	95	0.5	8.2	—	—	3.2	45.2	39.5	3.2	0.2
13-14 Yrs.	24	94	0.4	10.3	—	—	3.7	42.8	39.5	3.1	0.2
14-15 Yrs.	12	90	0.7	10.4	—	—	2.9	34.3	48.1	3.3	0.3
15-16 Yrs.	20	97	0.6	6.3	—	—	3.5	48.2	38.1	2.9	0.2
Over 16 Yrs.	13	97	0.2	8.0	—	—	3.7	42.0	43.2	2.8	0.1

AVERAGE VALUES FOR FEMALES

	cases	%	B	E	M	J	St.	S	L	Mo.	Pl.
2-3 Yrs.	17	83	0.3	2.6	—	0.4	6.6	38.1	45.7	5.3	1.0
3-4 Yrs.	21	92	0.2	3.6	—	0.1	4.4	36.5	50.4	4.0	0.8
4-5 Yrs.	15	82	0.3	6.0	—	—	3.8	38.7	47.8	3.4	1.0
5-6 Yrs.	19	88	0.2	7.8	—	—	3.2	37.0	47.6	3.6	0.6
6-7 Yrs.	8	92	0.3	5.6	—	—	2.9	35.9	51.4	3.3	0.6
7-8 Yrs.	3	95	0.3	6.3	—	—	3.1	31.2	51.6	4.1	0.4
8-9 Yrs.	12	95	0.4	8.9	—	—	2.7	40.1	44.6	3.1	0.2
9-10 Yrs.	9	94	0.8	5.8	—	—	3.4	45.6	40.4	3.6	0.4
10-11 Yrs.	15	98	0.6	8.0	—	—	2.8	42.9	42.0	3.4	0.8
11-12 Yrs.	12	94	0.8	8.1	—	—	2.9	38.4	45.3	3.3	0.2
12-13 Yrs.	21	95	0.3	7.8	—	—	3.4	45.0	40.0	3.3	0.2
13-14 Yrs.	11	99	0.3	6.7	—	—	3.2	38.7	47.4	3.3	0.4
14-15 Yrs.	7	97	0.4	6.5	—	—	3.0	43.3	43.8	2.7	0.3
Over 15 Yrs.	9	97	0.4	4.2	—	—	4.2	50.0	37.1	3.9	0.2

100% = 18,5 gr. Hemoglobin.

AVERAGE VALUES FOR BOTH SEXES

	Ages	No. of Cases	Hemoglobin	B	E	M	J	St.	S	L	Mo.	Pl.
			%	%	%	%	%	%	%	%	%	%
Maximum	2- 3 yrs.	32	102	2.0	8.0	—	3.2	13.2	54.4	70.0	13.6	3.6
Minimum			65	0.0	0.0	—	0.0	1.6	14.8	30.4	1.6	0.0
Average			78.5	0.25	3.45	—	0.3	5.3	34.75	49.65	5.15	1.15

	Ages	No. of Cases	Hemoglobin %	B %	E %	M %	J %	St. %	S %	L %	Mo. %	Pl. %
Maximum	3- 4 yrs.	40	107	1.2	15.2	—	1.2	10.4	68.0	76.8	6.0	2.4
Minimum			76	0.0	0.0	—	0.0	1.6	13.6	23.6	0.4	0.0
Average			91	0.25	4.25	—	0.05	4.35	38.25	46.45	3.65	0.8
Maximum	4- 5 yrs.	27	105	1.2	18.0	—	0.4	10.4	47.6	68.0	6.0	2.8
Minimum			70	0.0	0.0	—	0.0	1.6	24.4	35.2	1.6	0.0
Average			85	0.25	5.5	—	0.0	3.9	37.1	49.5	3.3	0.95
Maximum	5- 6 yrs.	35	104	1.6	18.4	—	0.8	6.0	54.4	67.6	6.4	1.6
minimum			74	0.0	1.2	—	0.0	1.6	20.8	36.4	2.4	0.0
Average			89	0.35	8.05	—	0.0	3.1	35.6	48.85	3.5	0.55
Maximum	6- 7 yrs.	25	104	1.6	12.5	—	—	5.6	50.6	72.4	6.4	1.6
Minimum			71	0.0	0.8	—	—	1.6	18.4	36.8	1.6	0.0
Average			92	0.35	5.7	—	—	3.1	37.45	49.65	3.45	0.5
Maximum	7- 8 yrs.	16	105	2.0	21.5	—	—	5.2	67.2	56.4	6.4	1.6
Minimum			67	0.0	0.8	—	—	1.6	15.6	18.8	2.0	0.4
Average			92.5	0.45	6.55	—	—	3.3	37.9	47.75	3.75	0.3
Maximum	8- 9 yrs.	29	105	0.8	24.0	—	—	6.5	58.4	64.8	5.0	1.6
Minimum			80	0.0	2.0	—	—	1.6	21.2	29.6	1.6	0.0
Average			94	0.3	7.55	—	—	3.2	41.3	44.5	2.9	0.25
Maximum	9-10 yrs.	27	105	1.6	27.0	—	—	7.0	61.6	68.0	5.2	1.2
Minimum			65	0.0	2.4	—	—	1.5	24.0	23.0	1.5	0.0
Average			93	0.55	7.25	—	—	3.4	48.85	41.35	3.3	0.3
Maximum	10-11 yrs.	38	106	1.6	19.2	—	0.4	6.5	58.2	57.0	6.0	1.6
Minimum			80	0.0	1.6	—	0.0	1.2	26.5	28.8	1.2	0.0
Average			95	0.6	8.25	—	0.0	3.15	40.65	44.0	3.2	0.25
Maximum	11-12 yrs.	31	105	2.8	19.2	—	0.4	6.0	64.0	70.4	6.0	0.8
Minimum			70	0.0	2.0	—	0.0	1.5	22.4	22.5	1.6	0.0
Average			92.5	0.6	8.05	—	0.0	3.25	41.8	42.95	3.25	0.2
Maximum	12-13 yrs.	42	110	2.0	20.4	—	—	4.5	60.0	57.6	6.0	1.2
Minimum			80	0.0	2.8	—	—	1.5	27.0	26.4	1.5	0.0
Average			95	0.4	8.0	—	—	3.2	41.95	43.45	3.25	0.3
Maximum	13-14 yrs.	35	110	2.0	33.6	—	—	9.0	55.0	57.6	5.0	0.8
Minimum			80	0.0	0.6	—	—	2.0	28.8	28.0	1.5	0.0
Average			96.5	0.4	8.5	—	—	3.35	41.75	43.45	3.2	0.3
Maximum	14-15 yrs.	19	105	1.6	22.4	—	—	4.8	44.8	58.0	6.0	2.0
Minimum			75	0.0	0.8	—	—	1.6	23.6	34.8	1.2	0.0
Average			93.5	0.5	8.55	—	—	3.05	36.55	47.75	3.3	0.35
Maximum	15-16 yrs.	27	105	2.0	21.5	—	—	6.4	62.0	50.8	5.2	0.8
Minimum			80	0.0	1.2	—	—	2.0	37.2	27.2	1.6	0.0
Average			95	0.5	4.95	—	—	3.55	50.3	37.55	3.4	0.2
Maximum	Over 16 years	14	105	0.8	14.4	—	0.4	8.0	54.5	51.6	4.5	0.5
Minimum			80	0.0	2.5	—	0.0	2.4	31.6	22.8	1.5	0.0
Average			97	0.3	6.1	—	0.0	3.95	46.0	40.15	3.15	0.1

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SIGNIFICANCE OF SOY BEAN IN THE DIETARY OF THE FILIPINOS *

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Soy bean, *Glycine max*, has been known for centuries in China and Japan. According to Adolph and Kiang [1] the use of soy bean in China dates back to the beginning of China's agricultural age under Emperor Shen Nung and it is mentioned in the Ben Tsao Yang Mu written by Shen Nung in the year 2838 B. C. When and by whom soy bean was first introduced in the Philippines is not known. However, the Filipino people have been known to use several important soy bean preparations such as soy sauce or "toyo", bean curd or "tokua," fermented bean curd or "tahuri", soy bean brain curd or "tojo", not knowing that they were prepared from this bean.

Soy bean is grown in many parts of the Philippines where it is known as "utao" and also as Chinese "Balatong." It is grown in large quantities in Batangas Province. The green pods are harvested in October and November and the dried seeds may be had in bulk in December and January. Just when soy bean was first cultivated in the Philippines is not known. For years casual plantings have been made but it is only in comparatively recent years that the cultivation has been seriously considered as an agricultural industry.

Statistics indicate that consumption of soy bean in the Philippines has grown faster than production. They also show a growing appreciation of soy bean in the Philippines. I am convinced, however, that greater efforts toward its popularization among the poor masses should be exerted, so that we can make it one of our national staple foodstuffs.

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* Read before the Sixth Pacific Science Congress, San Francisco, California, July 24 to Aug. 12, 1939.

The main purpose of the present paper is to show the importance of soy bean and soy bean products and to recommend its inclusion in the Filipino diet.

COMPOSITION AND NUTRITIVE VALUE

The first investigation carried out in the Philippines on the nutritive value of soy beans was made in 1912 by Gibbs and Agcaoili 2 of the Bureau of Science. They analyzed the soy bean curd made in the Philippines and described briefly the local method of manufacture. They also pointed out the fact that soy bean serves as an important nitrogenous food in countries like China and Japan where rice is the principal article of diet, and stated that the employment of this food was rapidly extending and its value becoming appreciated in other countries.

An investigation of the nitrogen content of soy bean imported into the Philippines was made by Brill and Alincastre 3 of the Bureau of Science in 1927. Field tests on the growing soy beans in the Philippines have been carried out by Layosa 4 who mentioned the fact that soy beans are used in China, Japan and other countries as a substitute for meat.

The composition of the Filipino soy bean compared with the American common varieties, is shown in table I.

TABLE I.—*Composition of Philippine and Foreign Soy Beans*

Variety	Moisture	Protein	Fat	N-free Nitrogen	Crude Fiber	Ash
	per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Philippine (a)	9.81	35.37	11.97	——	13.88	5.12
Philippine (b)	4.95	39.08	20.07	——	5.69	5.25
Ito san (c)	7.42	34.66	19.19	27.61	5.15	5.97
Haberlandt(c)	8.67	36.59	20.55	24.41	4.00	5.78
Midwest (c)	8.00	35.54	19.78	26.30	4.53	5.85

(a) Concepcion (1932) P.I.M.A., 12:97; (b) Cruz and West (1932) Phil. Jour. of Sci., 48:82; (c) Piper and Morse (1923). The Soybean.

As shown in table I, the Philippine soy beans have a higher calculated food value than any of the foreign beans.

The soy bean is characterized by its richness in protein, fat, and mineral matter, as can be seen in the comparison with other foods presented in table II.

TABLE II

Kinds of Foodstuff	Protein	Fat	Ash
Soy bean (*Glycine max*)	35.37	11.97	5.12
Black "patani" (*Phaseolus lunatus*)	8.87	4.43	3.66
Paayap pod (*Vigna sinensis*)	2.77	0.40	0.54
Mongo beans (*Phaseolus aureus*)	29.96	0.55	3.59
Eggs (hen)	12.57	12.02	1.07
Lean meat	19.30	16.70	0.90
Whole wheat	13.30	1.90	1.00
Cow's milk	3.89	3.90	1.80
Carabao's milk	4.97	6.84	0.81

The chief protein of soy bean is called glycinine, which is a complete protein, very similar in constitution to that of meat. It has properties similar to those of casein of milk, being coagulable by acid. According to Osborne and Mendel [5] glycinine differs from the protein of other leguminous ceeds in being adequate for promoting normal growth. It has been demonstrated that the human organism can store 3.3 per cent of the nitrogen taken in the form of soy bean curd, but only 1 per cent in the case of meat nitrogen. It has been shown by McCollum [6] that soy bean proteins fed to rats, in the proportion of 17 per cent can support growth.

Oshima,[7] in a summary of Japanese nutrition investigations gave as the average of two experiments, the coefficients of digestibility, 65 per cent for proteins, and 85 per cent for the carbohydrates of the soy bean. The first two experiments were made with beans simply boiled, the skin not being removed by cooking. In one experiment the quantity of beans eaten was very much larger than in the other, and the absorption was decidedly lower. The proteins of soy bean were found by Swaminathan [8] to be superior to those of green gram and lentil, and in this respect, soy bean appears to resemble the nuts and oily seeds. At a ten per cent level of protein intake, Swaminatan (loc. cit.) found that the digestibility coefficient and biologic value of soy bean were 76 and 54 respectively. As regards available or net protein content, the beans can be arranged in the following descending order: soy bean, green gram and lentil. It may be mentioned here, that in practical dietetics the quality of protein should be taken into consideration as well as the quan-

tity since all proteins especially vegetable protein are not of the same quality.

Very few people realize that soy bean is remarkable for its richness in oil, which averages about 20 per cent in some varieties. Crude soy bean oil can be digested by man to the extent of from 95 to 100 per cent. According to the studies of Korentschewski and Zimmerman [9] the presence of a considerable amount of linolic and linolenic acid in soy bean makes it exceptionally valuable for the building up of cell lipoids. The oil pressed or extracted from the bean has long been used in the Far East, and for the last few years has become the leading export of China. Besides its richness in oil, soy bean contains lecithin to the extent of 1.64%. It also contains cephalin, another phospholipid concerned in blood coagulation.

According to Osborne and Mendel [5], soy bean is the only seed thus far investigated that contains both the water-soluble and fat-soluble vitamins. On account of its richness in vitamin B_1 content, it is to be expected that if Filipinos would only consume it in much greater quantities than they do at present, it would help much in the prevention of beriberi in the Philippines.

In view of the importance that is attached to the mineral content of foods, several investigators have conducted studies on the ash content of soy bean. The ash of the soy bean has been found rich in phosphoric acid and potassium as shown in the analyses of Pellet [10].

It has been found by Duccheschi [11] that soy bean contains the following minerals: K — 2.095%; P — 0.64%; Na — 0.38%; Ca — 0.23%; Mg — 0.24%; S — 0.44%; Cl — 0.025%. It should be noted that there is more potassium than sodium in soy bean and this places it in the category of food alkalizing agent.

Since the ash of soy bean is strictly alkaline, the incorporation of soya flour with mixed diet neutralizes its acid components. In alkaline diet, "the organism is spared the necessity of providing ammonia to neutralize the inorganic acid obtained from the food" (Horvath). Moreover, the high alkalinity of soy bean is a very important factor for an optimal utilization of protein in the body. This may explain also why a human

organism can store three times as much nitrogen from soy bean as from meat (Rose and Macleod).

The calcium content of soy bean is 0.26%, whereas that of cow's milk is only 0.15% (Horvath). According to the same author [12] a soy bean diet, when supplemented by wheat flour reduces the percentage of fat in the mixture and brings the blood calcium to its normal level.

Data on the mineral content of the soy bean in comparison with the seed of three legumes generally used for food, are given in the following table:—

TABLE III.—*Mineral Content of the Soy Bean Seed Compared with those of Cowpea, Navy Bean and Peanut* *

Legumes	Potasium	Sodium	Calcium	Magnesium	Sulfur	Chlorine	Phosphoric Acid
	per cent	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*	*per cent*
Soy bean	2.095	0.380	0.230	0.244	0.444	0.025	0.649
Navy bean	1.390	0.086	0.235	0.206	0.254	0.047	0.429
Cowpea	1.636	0.189	0.117	0.243	0.280	0.047	0.532
Peanut	0.061	0.563	0.068	0.180	0.254	0.024	0.398

* Bowers (1919) Special Bull. N. D. Agric. Expt. Station, 5:13.

It will be noted in table III that the soy bean is second to navy bean in calcium but is richer than any of the others in potassium and phosphoric acid.

SUPPLEMENTARY VALUE OF SOY BEAN

So far, no investigations have been made in the Philippines to determine the supplementary value of soy bean in a diet consisting mostly of rice. However, experiments conducted in India by Swaminathan [13] on this question, using the nitrogen balance-sheet method on adult rats, showed that rice and soy bean are inferior to either rice and skimmed milk powder or rice and red gram. In another experiment in which the biologic value of the different mixtures was studied by the growth method, using young rats, Swaminathan (loc. cit.) found that at 8 per cent level of protein intake for a period of eight weeks, the following values were obtained; rice and skimmed milk — 1.86; rice and green gram — 1.29; rice and red gram — 1.26; rice

and Bengal gram — 1.21; rice and soy bean — 1.13; rice and black gram — 1.12

Experiments conducted in Japan by Izume and Komatsubaru [14] indicated that when 10% soy bean flour was used to supplement corn or rice, the results were quite satisfactory.

The result of the investigation of Concepcion and Paulino [15] with regard to the use of soy bean milk as a supplement to the ordinary diet of the Filipino children at Welfareville showed that its supplementary value is inferior to that of milk, and does not corroborate the results of Tso [16], or that of Guy and Yeh [17]. Whether or not this difference was due to insufficient amount of soy bean used cannot be ascertained; further work is necessary before this question can be answered. They have also come to the conclusion that soy bean milk cannot replace cow's milk in promoting growth in Filipino children.

FORMS OF SOY BEAN USED IN THE PHILIPPINES

There are several forms of soy bean used in the Philippines; among them may be mentioned soy bean curd or "tokua"; fermented bean curd or "tahuri"; soy bean brain curd or "tojo" and soy bean with ice shavings, "mongo con hielo." On the other hand soy bean milk and soy bean flour are practically unknown in the Philippines.

Soy Bean Curd or "Tokua"

One of the most important foods manufactured from the soy bean is the curd which is sold in the form of small cakes. Soy bean curd was first introduced in the Philippines by the Chinese and has become a very popular food in Manila and in places where there are Chinese who manufacture it. Soy bean curd, on account of its high fat, protein, and mineral salt content, is called by the Chinese "meat without bones," or "the poor man's meat."

This curd is known by a number of different names. In English, it is often spoken of as "bean-cake" or "bean cheese" although it is not entitled to the name "cheese," since no ripening process takes place in its manufacture. Attempts have been made to manufacture a cheese from the bean cake by means of inoculation with bacteria. Among the natives of the district of the Philippines surrounding Manila, it is called "tokua," a

name of Chinese origin. In China, the substance is known as "teou-fou" and "ta-hu" and in Japan as "tofu".

The chemical composition of soy bean curd prepared in the Philippines as compared with other preparations is shown in table IV.

TABLE IV.—*Composition of Soy Bean Curd*

Tokua	Fat	Protein	Ash	Carbohydrate	Water
Tokua (a)	10.99	17.56	1.27	——	72.10
Tokua (b)	3.67	10.11	0.35	3.24	81.87
Tokua (c)	3.38	6.29	0.58	1.64	88.11

(a) Gibbs and Agcaoili (1912); (b) Adolph and Kiang (1921); (c) Piper and Morse (1923).

In table IV it will be noticed that soy bean curd as prepared in the Philippines contains more proteins, fat and ash than those prepared in China and United States as reported by Piper and Morse [18].

The protein found in soy bean curd as reported by Matsuyama and Hashimoto [19] consists almost exclusively of glycinine. The nutritive value of soy bean curd is lower than that of the whole bean because it does not contain the water-soluble protein of the whole soy bean. The results of feeding experiments on soy bean curd carried out by the above investigators showed that when albino rats are fed with a mixture consisting of polished rice 80%, soy bean curd 17%, Osborne salt mixture, 2.18%, calcium carbonate, 0.2%, and a small amount of oryzanin, making the total protein content of the mixture 10%, the weight of the rats did not exceed 130 grams. When 5% of butter, however, was added to the ration, they began to grow vigorously. This means, according to them, that the protein was not inadequate but that the ration lacked the proper amount of fat-soluble vitamins. It may be stated further that soy bean curd, in the opinion of the above authors contains a large amount of magnesium so that the growth of the animal would be markedly interrupted unless a suitable amount of calcium was added to the ration.

The ash of the soy bean curd, according to an analysis based on the moisture-free sample performed by W. H. Adolph and C. M. Wu [20] contains 1.9 per cent of calcium oxide; 26 per cent

of magnesium oxide; 0.3 per cent of potassium oxide; 0.03 per cent of sodium oxide; 2.28 per cent of phosphorus pentoxide 0.01 per cent of iron. The coagulating medium used in the preparation of the curd analyzed was gypsum.

Fermented Bean Curd Or "Tahuri"

Another common preparation made from soy bean curd is "tahuri" or "tahuli". This was formerly manufactured in China and exported to the Philippines in large earthen jars or in small tin cans. At present there are several houses in Manila that manufacture "tahuri" for local consumption.

Those that are imported from China are preserved in strong brine solution and the cakes are broken during the shipment so the liquid becomes like a thick emulsion containing pieces of the cured curd.

In Manila, the Chinese method of manufacture is "to pack the large pieces of soy bean curd, about 5 inches long, 4 inches wide, and 2.5 inches thick, with much crude salt, in empty gasoline cans. The curd is allowed to cure for a period of several months. During the curing period, the bean curd changes from white to brownish yellow and develops a peculiar salty flavor to which the Chinese and many Filipinos are educated."

TABLE V.—*Composition of Tahuri* (a)

Tahuri	Water	Protein	Fat	Sodium Chloride
	per cent	*per cent*	*per cent*	*per cent*
Solid portion ...	55.76	14.56	7.12	12.70
Liquid	57.86	9.56	2.09	16.38

(a) Gibbs and Agcaoili (1912) Phil. Jour. of Sci. 7:47.

It will be noticed in table V that the protein and fat content of tahuri is less than the protein and fat content of soy bean curd (see table IV).

Soy Bean Brain Curd or "Tojo"

Another soy bean curd preparation known to many Filipinos is the so-called "tojo" or "taho". The method of making "tojo" is almost the same as that used in making "tokua", only that a smaller amount of the coagulating agent is used, and the

very soft but solid mass formed is left undisturbed in the wooden container until used. The Chinese used to peddle this preparation in wooden pail-shaped containers through different parts of Manila and the provinces, but on account of the Bureau of Health regulations, this product is now sold in the markets only.

The "tojo" is served with a few teaspoonfuls of medium thick brown-sugar syrup, which gives it a flavor, the "tojo" being almost tasteless. This preparation is very popular among the children and even adults as a breakfast food and it can be used as a substitute for soy bean milk.

Soy Bean with Shaved Ice or "Mongo con Hielo"

This is a very popular soy bean mixture introduced by the Japanese but now sold in nearly all refreshment parlors all over the Philippines. The preparation consists of a mixture of boiled red mongo and soy bean mixed with cream, brown sugar and ice shavings. This form of soy bean mixture is more nourishing than any other preparation just described on account of its cream and sugar content. Comparatively speaking, this preparation is more expensive than any other form because it is taken not with the meals but in between, in the form of refreshment.

Soy Bean Flour

Soy bean flour has been used for many years in America and Europe as a food for invalids and recently as a food for diabetics. This flour is made by grinding either the whole grain or the pressed cake remaining after the oil has been removed from the bean. It is on the market in the United States and is being put up like ordinary cereal flour. Several soy bean flours have been on the market in Europe and the United States during the last twenty years. It is to be regretted, however, that soy bean flour is still unknown in the Philippines except as a diabetic food. Efforts therefore should be exerted on the part of the authorities of this country to popularize among the masses the use of soy bean bread as a daily food in place of the whole wheat bread. The introduction of soy bean flour in the Philippines is very desirable because through its use the increasing importation of wheat flour can be greatly diminished. Steps in this direction are now being taken in the United States

and there is no reason why we should not follow the example of that country, expecially when we take into consideration that we are not manufacturing wheat flour in the Philippines. Such a step would mean a saving to us of many thousands of pesos and perhaps millions every year that could be very well used for other purposes which would lead to the betterment of the health of the people.

With regard to the digestibility of soy bean flour, Bowers [21] in his extensive investigation found that the protein of the soy bean flour, when thoroughly cooked, was about 91 per cent digestible by man, thus comparing favorably with the proteins of patent wheat flour. The carbohydrates, although consisting largely of dextrin, pentosan and galactan, were about 94 per cent digestible. John and Finks [22] using soy bean bread containing 25 per cent of soy bean flour found that the mixture of soy bean and wheat proteins is much better utilized than the wheat protein alone. Comparison shows that for the same amount of food consumed, the soy bean bread diet is about 2 or 3 times as efficient as the wheat bread diet.

Fiedenwald and Rurah [23] after conducting a series of investigations found that the soy bean flour is a valuable addition to the dietary of diabetics on account of its palatability and the numerous ways in which it can be prepared. They also found that the soy bean flour in some ways causes a reduction in percentage and total quantity of sugar passed in diabetic subjects under the usual dietary restrictions. In summer diarrhea and certain forms of intestinal disturbances, Rurah [24] found a weak gruel made from soy beans or preferably from gruel flour of the bean to be of great value. He found it to be generally well borne and digested by the children and rarely caused either vomiting or frequent bowel movements.

Soy Bean Milk

Soy bean milk is not a new thing. For centuries it has been used extensively in China and Japan where milk and its products are so scarce and so expensive that their use is limited. The use of soy bean milk could not have lasted that long if it had not been found to be satisfactory by generations of Chinese and Japanese.

The lack of cow's milk in the diet of the Filipino children is a serious handicap to their proper growth and development, resistance to disease and especially to the proper development of good, sound teeth that will resist early decay.

In European countries after the child is weaned, it is put to cow's milk which for a time constitutes its entire sustenance. As the child grows older and other foods are needed, the relative amount of daily milk given falls gradually. In the Philippines, the children of the poor, after weaning, do not taste milk except the little condensed milk they mix with coffee. Even with a well-selected diet, it is doubtful whether a child can obtain maximum growth and development without the use of milk. It is for this reason that the maintenance of an adequate milk supply in this country, especially in the provinces, at as low a price as possible, becomes a matter of much more than nutritional importance.

In China and in Japan, many factories are dedicated to the manufacture of soy bean milk. The Chinese and Japanese people use it for drinking purposes and for infant feeding. A small quantity of sugar is added to the milk when it is used as a beverage.

As a substitute for cow's milk, Tso [25] has proved that soy bean milk when properly supplemented can support normal growth in infants. He fed an infant, six weeks old, a diet in which no milk was included other than soy bean milk supplemented with sugar, orange juice, cod-liver oil, egg, rice porridge, spinach puree and sodium chloride. He found that the infant thrived well and steadily gained in weight during eight months. Furthermore, he observed that the infants compared favorably in height and weight with infants that were breast fed.

Guy and Yeh [17] also reported a successful feeding of infant with soy bean milk reinforced with calcium lactate, sodium chloride, starch sugar, cabbage soup, and cod liver oil to supply vitamins A, C and D. None of the infants exhibited anaemia but they showed less muscular vigor than those who were fed entirely on maternal milk.

A recent quantitative estimation [26] showed that soy bean milk contained three times as much vitamin B_1 and only two times as much vitamin B_2 as does dried cow's milk.

Hill and Stuart [27] in feeding 40 babies with soy bean milk indicated that the babies thrived. They took it well, digested it, and gained weight on it. Since soy bean milk is inferior to cow's milk in mineral content, the addition of 2 grams of calcium carbonate and 1 gram of sodium chloride to every 100 grams of soy bean used for making milk is necessary according to them, if the child is to be entirely dependent on the milk for its food supply.

In addition to its value as food for both young and old, soy bean milk also serves to check the summer diarrhea common to children. Sinclair [28] in his experiments on babies who had diarrhea and intestinal disturbances, found soy bean milk to be very useful in curing the majority of cases.

It may be of interest to show the composition of soy bean milk as compared with either cow's or human milk.

TABLE VI.—*Comparative Composition of Soy Bean Milk, Cow's Milk and Human Milk*

	Soy Bean Milk	*Cow's Milk*	*Human Milk*
Moisture	91.89%	87.27%	87.58%
Proteins	4.40	3.39	2.01
Fat	1.80	3.68	3.74
Carbohydrates	1.50	4.94	6.37
Ash	0.41	0.72	0.30
Calcium	0.015	0.12	0.40
Phosphorus	0.05	0.09	0.10

It can be readily seen in table VI that soy bean milk does not differ very much from either cow's or human milk. Its chief defect lies in its low content of fat and carbohydrates which is remedied by the addition of either sugar or starch or both in sufficient amounts. In protein content, it is slightly superior to either, and in ash or mineral content it has about the same amount, although poorer in calcium and phosphorus. When properly supplemented, therefore soy bean "milk" closely resembles mammalian milk, although the cost is only a fraction of that of the latter.

For many years, our nutritionists have been working to solve the milk problem in the Philippines. On account of its high cost, milk is not within the reach of the poor class of peo-

ple, and until the time comes when we have increased milk supply, the use of soy bean milk, at least for our children population, should be tried as a temporary solution.

DEFICIENCIES OF FILIPINO DIET

It is now an admitted fact that the Filipino diet is deficient in several respects, among which may be mentioned, the deficiency in vitamins A and B_1, low fat, deficiency in calcium and iron, and deficiency in animal protein. The reasons for the deficiency are manifold, the low income of the people, which prohibits the purchase of food of high nutritive value such as milk, eggs, meat, etc. and their ignorance of food values. Polished rice is the principal food of the Filipino people, which consists mostly of starch, deficient in protein, mineral salts, especially calcium and phosphorus, and vitamins, particularly vitamin A B_1 and C. Animal protein, as already stated, is deficient in the diet of the poor. It is to those people who cannot well afford to buy expensive animal protein that the liberal use of soy bean is strongly recommended. Experiments made by some nutritionists indicate that 20 per cent of soy bean and 80 per cent rice make a well balanced diet as far as protein and fat are concerned, and in order to increase the vitamin and mineral content of the diet, especially vitamin A and calcium, green leafy vegetables and fruits should be incorporated in it.

In considering a suitable diet for the poorer classes of people, the question of cost is always of paramount importance. The current price of soy bean in the Islands at the present time is less than that of rice. If it is grown more extensively than at present its cost would certainly be less, and by substituting part of the rice in the diet with soy bean, the nutritive value of the diet will not only be increased but the actual cost of it will also be decreased.

EFFECTS OF IMPROPER FOOD

There is abundant evidence to warrant the conclusion that food of improper constitution, especially when it is deficient in vitamins, is responsible for a large proportion of ill health in this country. It has been pointed out time and again that partial deficiency in some food essentials particularly in vitamins and mineral elements, is much more widespread among our peo-

ple than the actual deficiency diseases, and that this partial deficiency leads to a lowering of vital processes, to impaired resistance against microbic infection, and to the development of diseases of many kinds. One of the consequences of the inadequate intake of vitamin B_1, one of the most common error in the Filipino diet, is beriberi. This is due to extensive use of white polished rice and to the excessive use of other foods rich in carbohydrates. The mortality rates of beriberi from 1925 to 1937 both in infants and adults are shown in table VII.

TABLE VII.—*Showing Number of Deaths Due to Beriberi and Death Rates Per 100,000 Population from 1925 to 1937* *

Year	No. of Deaths Infant	Mortality Rates	No. of Deaths Adult	Mortality Rates
1925	12,878	124.24	1,519	14.67
1926	14,027	133.51	5,182	49.32
1927	12,575	118.00	4,500	42.23
1928	12,291	113.74	4,492	41.57
1929	15,141	138.19	5,084	46.40
1930	16,485	148.42	5,089	45.82
1931	15,018	133.41	4,520	30.15
1932	13,302	116.62	3,871	33.94
1933	14,720	127.37	3,962	34.28
1934	17,054	131.90	4,365	33.76
1935	14,299	109.16	4,315	32.94
1936	11,316	85.30	3,502	26.40
1937	13,004	96.80	3,793	28.23

* Taken from the records of the Bureau of Health.

The mortality due to infantile beriberi exceeds by a large margin that from the others. The rates range from 85.30 per 100,000 population in 1936 to 148.42 per 100,000 population in 1930. From 1925 to 1934, the rates are rather irregular but do not show any tendency to diminish, averaging 128.55 per 100,000 population. However, we notice a decrease in 1935 to 109.16, in 1936 to 85.30 and in 1937 to 96.80 per 100,000 population. Beriberi has also claimed its toll among adults, the mortality rates varying from 14.67 per 100,000 population in 1925 to 49.32 per 100,000 population in 1926. This means that there was a marked increased in the death rate from 1925 to 1926, then from 1926 there is an irregular drop in the mor-

tality rate as we approach 1937, although not to as low as a level as in 1925. The death rate in 1937 from this disease in both adults and infants is still high, although there was an appreciable tendency to diminish during the years just previous.

THE NEED FOR A CAMPAIGN TO POPULARIZE SOY BEAN PRODUCTS

Although several soy bean preparations are known to the Filipinos, such as soy sauce, bean curd, fermented bean curd, soy bean brain curd, etc. their consumption does not amount to very much. The reason for this apparent neglect is the general lack of sufficient information. It is desirable that the government should initiate the necessary campaign to inform the people regarding the valuable nutritive properties of soy bean. Although the Bureau of Science since 1931 has been carrying a demonstration campaign to teach the public the different methods of cooking soy bean with the aim of popularizing its use among the masses, its efforts so far have not yielded the expected results. Another reason is the lack of a central body in the Philippines that can coordinate all the nutrition work to be carried out in that country. Furthermore, there is lacking a definite long range policy for the betterment of nutrition. People become rigidly bound by custom and necessity to certain eating habits many of which may be detrimental to their own welfare and hence to the welfare of the nation. It takes a definite and vigorous policy, pursued over an extended period of time to overcome and correct these habits, supplemented with improvements in the quantity and type of agricultural products, all of which take time and sustained effort.

The popularization among the masses of soy bean and soy bean products like soy bean curd, soy bean flour, and soy bean milk should be undertaken along with a more intensive campaign about its nutritive value carried on in the different schools all over the Philippines.

CONCLUSIONS

There is a marked deficiency of protective foods in the diet of the common masses of the Filipinos on account of their low incomes which prevents them from getting the necessary amount of these kind of foods. It is also on account of their ignorance

of food values, that the use of protective foods like milk, eggs, vegetables and fruits is neglected. Since soy bean is found to be rich in those constituents that are deficient in the ordinary Filipino diet, namely vitamins, minerals and fat, and on account of its moderate cost, it is possible for people of small incomes to obtain it without much difficulty.

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THE FREEZING POINT OF CARABAO'S MILK AND ITS USE IN THE DETECTION OF ADDED WATER[1]

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The most nearly constant of the properties exhibited by cow's milk is its freezing point (Woodman, 1931). This physical constant was found to vary only within narrow limits. Pins (cited by Associates of L. A. Rogers, 1928) found a variation of from —0.529°C. to —0.569°C. in 1940 samples obtained from 25 cows. In recent years extensive investigations by Hortvet, Bailey and others show the limits to be —0.530° and —0.566°C. for normal individual cows and —0.530° to —0.562°C. for milk from normal herds (Leach, 1936). A variation of only 0.016°C. was found by Schuette and Huebner (1933) in milk from the same herd. It is thus the fairly constant value of the freezing point of cow's milk which makes it a reliable index of the presence of added water in milk, for the other factors that ordinarily affect the chemical composition of milk —like the breed of cows, individual differences, the time of milking, the portion of the milk, the stage of lactation, the kind and quality of food, etc.—do not affect it significantly (Associates of L. A. Rogers, 1928; Leach, 1936).

The method of detecting watered milk by the determination of its freezing point was first suggested by Beckman in 1894 (Cited by Leach, 1936), when he found that water influenced the freezing point of milk in proportion to the amount added. Since then the literature on the application of the freezing point determination for the detection of this form of milk adulteration has grown to voluminous proportions. It is not the purpose of this paper, however, to review such literature, but merely to point out a few salient facts that have been brought out by these studies.

[1] Done under the direction of Dr. P. I. de Jesus, Acting Head of the Nutrition Laboratory.

It appears that the lower freezing point of milk compared to water, or in other words the depression of the freezing point, is due to dissolved substances (Associates of L. R. Rogers, 1928) and that insofar as freezing point determination is concerned milk may be considered a water solution of sugar and salts. The addition of water to milk would then, of course, result in the approximation of its freezing point to that of water. Staub (loc. cit.) believes that the depression of the freezing point must be due to three factors: the chlorine (chloride), the sugar and a group of residual substances. The suspended solids, i.e., the fats and the proteins, exert either no influence at all or only a slight and practically negligible effect according to most authors (Leach, 1936).

The reason for the narrow variation of the freezing point values of milk lies in the fact that the osmotic pressure of the milk depends on that of the blood (Jackson and Rothera, cited by Associates of L. A. Rogers, 1928), since it was found by osmotic pressure measurements that the milk is isotonic with the blood (Stoecklin, Mundala, loc. cit.). Osmotic pressure may be indirectly measured by the depression of the freezing point, and if milk is isotonic with blood, they should have the same freezing point, which agreement was observed by van der Loon, Winter, Stoecklin and Mundala (loc. cit.). Blood is characterized by a remarkably constant osmotic pressure, and therefore a constant freezing point value. Milk being isotonic with blood must share this property.

Since the freezing point of cow's milk has been found to be the most nearly constant of the properties exhibited by milk and for this reason has been employed in the detection of added water, it seemed worthwhile to find out if the same holds true in the case of carabao's milk which is more commonly consumed in the Philippines than cow's milk.

MATERIALS AND METHOD

The samples of carabao's and cow's milk examined in this investigation were obtained from the Alabang Stock Farm of the Bureau of Animal Industry. These samples consisted of pooled raw milk from the herd. Milking was done early in the morning and the milk reached the laboratory about two hours

later. Determinations of the freezing point were done on the samples upon receipt without much delay.

For these determination the Hortvet Cryoscope, the apparatus adopted by the Association of Official Agricultural Chemists (1935), was employed. The official cryoscopic method was followed strictly with one single exception. It was found that the manner of starting the freezing action in the milk by the official cryoscopic method was not always sure of action. Instead of using the freezing started in the manner described in the official method, freezing was initiated by dropping into the freezing test tube a small fragment of ice with the aid of forceps. The standardization of the thermometer was done only once using solutions prepared from a pure sample of sucrose (Saccharose, Difco), but the zero error was determined every time before the freezing point determinations for the day were started.

RESULTS AND DISCUSSION

The Average Freezing Points of Carabao's and Cow's Milk

The freezing points, or more commonly called freezing point depressions (F.P.D.), of a total of 16 samples each of carabao and cow's milk were determined. The average F.P.D. obtained for carabao's milk was —0.539°C. ± 0.00097°C. (S.E.); the minimum observed being —0.527°C. and the maximum —0.545° (table 1). For cow's milk the average F.P.D. found was —0.542°C ± 0.00218°C. (S.E.); the minimum observed being —0.531°C. and the maximum, —0.560°C (table 1). The difference between the average F.P.D.'s of carabao and cow's milk was not found to be statistically significant.[1] While the size of the sample does not warrant a definite conclusion it is very likely that even if we increase the size of the sample to include the milk from other herds in the Philippines the same relation will be found.

The Relation of the F.P.D. to the Composition of Milk

The same samples whose F. P. D.'s were determined were analyzed for total solids, and fat (A. O. A. C., 1935) and by difference the solids not fat was computed.[1] From the com-

[1] I am thankful to Mrs. P. S. Suaco, Analyst of the Food Laboratory, for her help in the determinations of solids, fats and acidity.

puted coefficients of variation (table 1) it is seen that the F. P. D. is much less variable than the total solids and the two components of the total solids, e.g. the fat and the solids not fat which are the basis of the standards for milk in the Philippines (Board of Food Inspection, 1932), or that the F. P. D. is very neatly constant in spite of considerable variations in the composition of milk. This greater variability of fat and solids not fat of milk made them less satisfactory as standards for the purity of milk. Thus the sample which gave the minimum values of 6.34 per cent of fat and 6.80 per cent solids not fat for carabao's milk, and 2.82 per cent of fat and 7.48 per cent solids not fat for cow's milk would have been deemed adulterated by the addition of water had they been judged merely by their content of fat and solids not fat alone, even when such samples were pure unadulterated milk. It is noteworthy also that even if the averages for total solids, fat and solids not fat of the samples of carabao and cow's milk differed significantly those for their F.P.D.'s did not. This would seem to indicate that the F. P. D. is very insignificantly if ever influenced by the fat and solids not fat in milk. To study the matter further the coefficients of correlation were determined and the results are shown in table 4. The coefficients of correlation obtained show that there is hardly any correlation at all, and the values found are only slightly better than zero or no correlation. This is further proof of the lack of influence of the fat and solids not fat on the F. P. D. which is true at least as far as the limits of these constituents in the samples analyzed.

The Influence of the Addition of Water to the F. P. D.

To determine the influence of the addition of water to the F. P. D. of milk observations were made of the F. P. D.'s of carabao and cow's milk to which 0, 5, 10, 20, 30, 40 and 50 per cent of water by weight were added. A total of 9 samples each of carabao and cow's milk were studied in this manner giving average F. P. D.'s shown in table 2. When the average F. P. D.'s were plotted as ordinates and the per cent of added water as abscissae two very nearly straight lines for the two milks were obtained showing that there is a straight-line rela-

tionship between the F. P. D. and the per cent of added water which relation can be expressed by the equation:

$$Y = a + bX$$

which means,

F. P. D. = a + b (per cent added water)

The constants a and b were determined arithmetically by the "method of least squares" giving two equations (fig. 1):

Carabao's Milk: $Y = -0.5318 + 0.0057\ X$ (1)

Cow's Milk: $Y = -0.5375 + 0.0056\ X$ (2)

These equations give the freezing points in °C. (Y) estimated as most likely to be obtained on the average from the addition of 0 per cent to 50 per cent of water by weight (X). From these equations every addition of 1 per cent by weight of water causes a rise of 0.0057°C. and 0.0056°C. of the freezing points of carabao and cow's milk respectively. Determinations with the Hortvet Cryoscope are accurate within ± 0.002°C. so that these changes in the freezing points can very well be detected. Winter's data (cited by Associates of L. A. Rogers, 1928) show that for each addition of one per cent by volume of water there is a rise of approximately 0.0055°C in the freezing point of cow's milk which value is almost identical with that obtained in this investigation. If no water is added one should expect a freezing point of —0.5318°C for carabao's milk and —0.5375°C. for cow's milk.

From regression equations (1) and (2) regression lines have been drawn (chart 1) which describe the relation between the addition of water and the estimated freezing point or F. P. D. These regression lines may be used to estimate the per cent of added water given the freezing point of a sample of carabao or cow's milk. Values beyond 50 per cent of added water may be approximately determined by extrapolating these lines, although such values will not be as reliable as those within the limits of 0 to 50 per cent.

The per cent of added water on the average may also be estimated mathematically by the equation:

$$X = a + b\ Y$$

where X (per cent of added water) is now the dependent factor.

Solving for the constants a and b the following equations are obtained:

Carabao's Milk: $X = 93.1909 + 175.1546\ Y$ (3)

Cow's Milk: $X = 96.2629 + 179.2416\ Y$ (4)

Equations (3) and (4) may now be used to estimate mathematically the per cent of water that was added to a sample of milk once its freezing point has been determined.

The estimated values of the per cent of added water will not, however, in many cases coincide with the actual values. To illustrate this the observed F. P. D.'s corresponding to 0, 5, 10, 20, 30, 40, and 50 per cent added water were compared with the estimated values calculated from equations (1) and (2), and the results are tabulated in table 3. It is seen from the table that in no instance was there perfect agreement between the estimated and the observed values; small differences exist between these two sets of values. Thus it is necessary to establish a range for the estimated values within which we should expect the observed values to fall. Calculation of the standard deviation of these differences, called the standard error of estimate (Ezequiel, 1930), gives the desired figures. For carabao's milk the standard error of estimate found was $\pm 0.0054°C.$; for cow's milk, $\pm$ 0.0021°C. These values added and subtracted from the estimated values give us a range within which two-thirds of the observed values would be expected to fall. But it is desired that the range should be such as to include with almost perfect certainty all the observed values, and for this reason it is more preferrable to use values three times the standard error of estimate. Three times the standard error of estimate was found by computation to correspond to a difference of approximately $\pm$ 3 per cent of added water. A tolerance of $\pm$ 3 per cent must, therefore, be allowed on the estimated values of the per cent of added water to milk. Further, if a sample of carabao or cow's milk is found by determination of its F. P. D. to contain more than 3 per cent of added water it is practically certain that the sample has been adulterated by the addition of water.

The Influence of Acidity on the F. P. D.

It is one of the requirements of the determination of added water in milk by the freezing point method, also called the

cryoscopic method, that the milk so examined must be fairly fresh. It is recommended that the acidity should not exceed 0.18 per cent reckoned as lactic acid (Cox, 1938; A. O. A. C., 1935), for souring lowers the freezing point of milk (Bonnema and Keister, cited by Leach, 1936).

The F. P. D. and the acidity reckoned as lactic acid of 15 samples of fresh undiluted carabao and cow's milk were determined and the results are shown in table 5. The acidities range from 0.154 to 0.250 per cent for carabao's milk and 0.138 to 0.210 per cent for cow's milk. A mere inspection or these figures fails to reveal any apparent correlation between the F. P. D. and the acidity of the milk, i.e., decreasing values of the F. P. D. do not correspond with increasing values of the acidity. Coefficients of correlation calculated from these figures were 0.54 for carabao's milk and 0.07 for cow's milk which were not found to be statistically significant. Probably, therefore, within the limits mentioned above, acidity did not influence significantly the F. P. D. It would have been better, of course, to follow the change in the F.P.D. of samples of carabao and cow's milk allowed to develop acidity. Data so obtained would be more conclusive.

The Influence of Other Factors on the F. P. D.

According to Gooren (Leach, 1936) the processes of homogenizing, pasteurizing and sterilizing milk lowers its freezing point although his findings have not been corroborated by other investigators. The addition of certain preservatives and common salt also lowers the freezing point (Bonnema and Keister, cited by Leach, 1936). Hence, it is recommended that in order to obtain reliable results milk that is to be examined for the addition of water by the cryoscopic method must be free from these substances. The influence of these factors were not studied in this investigation. There is every reason to believe, however, that the latter substances when added to milk will lower or depress its freezing point. It would be interesting, too, to find out the effect the addition of coconut "milk" would have on the freezing point, coconut "milk" being a common adulterant of milk in the Philippines.

SUMMARY

1. The average freezing point depressions (F. P. D.) of 16 samples each of carabao and cow's milk were $-0.539°C \pm 0.0000$-97°C and $-0.542°C \pm 0.00218°C$ respectively. The difference between these figures was not statistically significant.

2. The addition of water to carabao and cow's milk produced a rise of the F. P. D. proportional to the amount of water added. From this relation regression lines and equations were determined by means of which the per cent of water added may be estimated. A tolerance of 3 per cent added water is recommended. If a sample of carabao and cow's milk when subjected to the cryoscopic method is found to contain more than 3 per cent added water it is practically certain that water has been added to the milk.

3. The fats and solids not fat were shown to be less reliable as indices for the presence of added water in milk. These constituents were also shown to have no influence on the F. P. D. of carabao and cow's milk. Acidity within the limits observed in this investigation (0.154 to 0.250 per cent for carabao's milk, and 0.138 to 0.210 per cent for cow's milk) exerted none or only a negligible influence on the F. P. D.

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TABLE I.—*Comparison of the statistical constants of the freezing point depression (F. P. D.), acidity, total solids, fat, and solids not fat of carabao's and cow's milk.*

	F. P. D.		ACIDITY		TOTAL SOLIDS		FAT		SOLIDS NOT FAT	
	Carabao	Cow	Carabao	Cow	Carabao	Cow	Carabao	Cow	Carabao	Cow
Minimum	—0.527	—0.531	0.154	0.138	17.67	11.35	6.34	2.82	6.80	7.48
Maximum	—0.545	—0.560	0.250	0.209	23.68	14.77	11.26	6.34	14.88	10.18
Average	—0.539	—0.542	0.184	0.166	20.52	13.63	8.95	4.47	11.57	9.15
Standard Deviation	0.004	0.009	0.027	0.020	2.03	0.79	1.57	0.69	1.62	0.68
Coefficient of Variation	0.72%	1.66%	1.47%	1.21%	9.91%	5.78%	17.53%	15.50%	13.95%	7.47%
Standard Error	+0.00097	+0.00218	+0.0072	+0.0053	+0.5253	+0.2035	+0.4052	+0.1790	+0.4171	+0.1767
Difference	0.003		0.018		6.89		4.48		2.42	
Difference ∂ diff.	0.40		2.02		12.23		10.11		5.34	
p	0.689		0.043		<0.0001		<0.0001		<0.0001	
Significance	not significant		significant		significant		significant		significant	

Values of p obtained from Pearl's "Introduction to Medical Biometry and Statistics" 3rd. ed. rev. enl. W. B. Saunders Company, Philadelphia and London, 1940.

TABLE 2.—*Elevation of the freezing point depression (F.P.D.) upon the addition of water to carabao's and cow's milk*

Per Cent Added Water	No. of Samples	Average F. P. D.	
		Carabao's Milk	Cow's Milk
		°C.	°C.
0	9	—0.5382	—0.5403
5	9	—0.5052	—0.5091
10	9	—0.4714	—0.4787
20	9	—0.4132	—0.4236
30	9	—0.3558	—0.3694
40	9	—0.3009	—0.3137
50	9	—0.2547	—0.2599

TABLE 3.—*Differences between observed and estimated F.P.D.'s of carabao and cow's milk*

Per Cent Added Water (X)	Observed F.P.D. (y)		Estimated F.P.D.* (y')		Difference between Observed Over Estimated (z)	
	Carabao's Milk	Cow's Milk	Carabao's Milk	Cow's Milk	Carabao's Milk	Cow's Milk
	°C.	°C.	°C.	°C.	°C.	°C.
0	—0.5382	—0.5403	—0.5318	—0.5375	—0.0064	—0.0028
5	—0.5052	—0.5091	—0.5033	—0.5095	—0.0019	+0.0004
10	—0.4714	—0.4787	—0.4748	—0.4815	+0.0034	+0.0028
20	—0.4132	—0.4236	—0.4178	—0.4255	+0.0046	+0.0019
30	—0.3558	—0.3694	—0.3608	—0.3695	+0.0050	+0.0001
40	—0.3009	—0.3137	—0.3038	—0.3135	+0.0029	—0.0002
50	—0.2547	—0.2599	—0.2468	—0.2575	—0.0079	—0.0024

* Computed by regression equations:

Carabao's Milk: $Y = 0.5318 + 0.0057\ X$

Cow's Milk: $Y = 0.5375 + 0.0056\ X$

TABLE 4.—*Correlation of the F.P.D., acidity, fat and solids not fat of carabao and cow's milk.*

FACTORS CORRELATED	CARABAO'S MILK		COW'S MILK	
	Coefficient of Correlation	Significance	Coefficient of Correlation	Significance
F.P.D. and Acidity	+0.54	not significant	+0.07	not significant
F.P.D. and Fat	—0.54		—0.21	
F.P.D. and Solids Not Fat	+0.16		+0.07	

* When the ratio of the S.E. of the coefficient of correlation of the observations over the S.E. of no correlation was 2 or more the correlation was considered significant.

TABLE 5.—*Relation of Acidity to the F.P.D.*

CARABAO'S MILK		COW'S MILK	
F. P. D.	Acidity	F. P. D.	Acidity
°C.	*per cent*	°C.	*per cent*
—0.527	0.195	—0.531	0.165
—0.536	0.250	—0.531	0.138
—0.536	0.154	—0.531	0.160
—0.538	0.226	—0.533	0.149
—0.538	0.209	—0.535	0.154
—0.539	0.160	—0.536	0.210
—0.540	0.183	—0.536	0.209
—0.540	0.165	—0.537	0.171
—0.540	0.198	—0.541	0.182
—0.541	0.170	—0.542	0.165
—0.541	0.170	—0.543	0.149
—0.541	0.165	—0.551	0.192
—0.541	0.171	—0.553	0.165
—0.542	0.193	—0.556	0.150
—0.545	0.158	—0.560	0.171
Coefficient of Correlation 0.54		Coefficient of Correlation 0.07	
Not significant		Not significant	

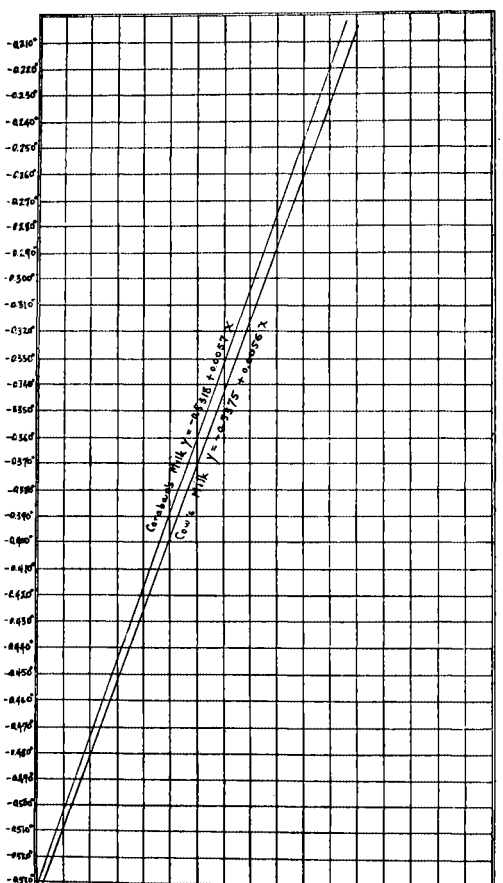

Chart 1. Regression lines and equations for the effect of the addition of water on freezing point of carabao's and cow's milk.

ANOMALOUS ORGAN-LOCALIZATION OF *SCHISTOSOMA JAPONICUM* IN EXPERIMENTALLY INFECTED MONKEYS (*MACCACUS CYNOMULGUS*)

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In their extensive experimental infection of dogs with *Schistosoma japonicum* Faust and Meleney [3] observed that in this animal the jejunum was the portion of the alimentary tract most intensely involved. Lesions were progressively fewer in number through the ilium toward the colon and were uncommon in the duodenum. Although the colon was slightly involved they are more inclined to attribute the intense congestions found in the mucosa of this organ to the congestion of the larger inferior mesenteric veins which often contained many worms. The stomach occasionally showed isolated lesions due to egg deposits, and in hyperinfected dogs the gastric veins were crowded with worms. This distribution of intestinal lesions is in contrast to that found in human infections, where the colon is the part most involved.

We once exposed a Philippine monkey (*Maccacus cynomulgus*), to the cercariae of *Schistosoma japonicum;* the animal died of toxic dysentery 35 days after infection. On autopsy we observed that in this monkey, contrary to the findings of Faust and Meleney [3] in the dog, the lesions were mostly in the large intestine scattered here and there from the caecum to the rectum, the small intestine being only slightly involved. The distribution of intestinal lesions in the monkey seems to approximate more closely that observed in human infection, if it is not altogether identical. This finding has led us to perform a more extensive experimental infection of this animal with *S. japonicum* with the object in view of obtaining further information concerning the organ-localization of this important human blood fluke.

This paper which is a partial report on the results of our preliminary experiments will deal mainly with the unusual finding of sexually mature egg-laying specimens of *Schistosoma japonicum* in the vena cava and right chambers of the heart of two out of four of our monkeys experimentally infected with the cercariae of *Schistosoma japonicum* both of which died with symptoms of toxic dysentery 49 days and 51 days after infection.

PROTOCOLS

Monkey No. 2 Re—A male monkey caught in Indang, Cavite, weighing about 2.5 kg. was prepared for artificial infection with cercariae of *Schistosoma japonicum.* Examination of the feces revealed eggs of hookworm and many cysts of Entamoeba sp. On August 19, 1940, one hundred and five cercariae from crushed snails (*Oncomelania quadrasi*) which were collected from the vicinity of Lake Mainit, Surigao, were applied for about one hour on the abdomen of the animal while it was held in recumbent posture. Two days later 639 more cercariae were applied in the same way. Many pinkish papules were observed on the site of inoculation about 24 hours after the last application of larvae. These papules remained visible for four days. Differential counts made every other day from August 22, 1940 to September 30, 1940 showed an average eosinophile percentage of 20 per cent. During this period, the monkey was apparently strong, very active and had good appetite. On October 1, 1940, the stool became flecked with blood and mucus. Examination of the bloody-mucoid portion of the stool showed abundance of *Schistosoma japonicum* eggs. Differential count done on this day showed only 3 per cent eosinophiles. The animal was not so active and seemed to be weak as shown by the little resistance he offered when taken out of the cage. Since then bowel movements became more frequent and the scanty stools consisted mostly of blood and mucus with very little fecal matter. Numerous eggs of *S. japonicum* were invariably present each time fecal examination was made. The animal became very ill on Oct. 4 and rapidly grew weaker and weaker until it finally succumbed on Oct. 9 prodigiously passing out blood and mucous up to the last moment of life.

Autopsy findings: Body of a greatly emaciated monkey with the perianal region thickly smeared with bloody-mucoid stool which still continued to exude from the anus. On opening the peritoneal cavity, we noticed no fluid but the small and large intestine were distended. At two points the lower margin of the great omentum was adherrent to the descending colon. The liver was markedly enlarged with a somewhat granular surface. The large intestine from the caecum to the rectum was markedly congested, the walls thickened and rough; the small intestine was only markedly congested and free from adhesions. Dissection of the portal veins and its principal tributaries yielded thirty adult male and female specimens of *S. japonicum*. The liver was somewhat resistant to sectioning. Thirty more adult male and female worms were squeezed out from its cut surface. The spleen was apparently not enlarged although its color was grayish-black. On opening the large intestine the whole mucosal surface from the caecum down to the rectum appeared almost denuded due to the numerous minute ulcerations which in nearly four-fifth of the area were confluent and covered with pseudo-diphtheritic membranous exudate not unlike what is frequently found in acute bacillary dysentery colitis. Scrapings from this area showed innumerable eggs on examination. No ulcerations were found in the small intestine.

The heart and lungs were moderately congested. When the heart was opened, a couple of sexually mature worms still in copulation was found enmeshed in a large fibrinous clot in the right auricle; and just below the tricuspid area, an adult male specimen was found entangled among the chorda tendinae. Dissection of the pulmonary artery and veins of the lungs was done but no worms were found. The heart showed no other signs of abnormality both macroscopically and histologically. Histological sections showed that the liver and large intestine were extensively damaged with heavy infiltrations of eggs and the characteristic egg-abscesses and pseudotubercles were abundant especially in the portal tissue. The extensive destruction of the mucosa of the large intestine was even more apparent in histological sections in which groups of eggs radiating out in rows toward the intestinal lumen in the stroma

of the mucosa from a central point in the submucosa were frequently observed, exactly as Faust and Meleney 3 described in their monograph. No eggs were found in histological sections of the brain, kidneys, spleen, lungs and myocardium.

Monkey No. 3 Sn: A male monkey from Indang, Cavite weighing about 3 kg. Feces showed Trichuris eggs and many Entamoeba cysts at the start of the experiment. Following the same method used above, 221 cercariae obtained from crushed snails (*Oncomelania quadrasi*) collected from Palo, Leyte, were applied on the animal's abdomen on September 14, 1940. Many pinkish papules were also observed on the site of larval application about 24 hours after. These papules remained visible for about a week but vesicle formation was not observed. Differential counts made at intervals of from two to three days from Sept. 17 to Oct. 16, 1940 showed a gradual increase in eosinophiles from 3 per cent to 22 per cent. Except for the poor appetite observed during the week previous to the onset of dysenteric symptoms, the animal was apparently strong and active. On Oct. 17, 1940, the first bloody-mucoid stool with abundant *Schistosoma japonicum* eggs was passed out. On this day the monkey was noticeably weaker. Differential count showed a sudden drop of the eosinophile percentage to 3 per cent. Since then the bowel movements became more frequent, and the stools more scanty, at times mixed with a little fecal matter but most of the time consisting of pure blood and mucus, which on examination always showed abundant eggs. On Oct. 26 the monkey could hardly move its limbs, was very pale and emaciated and did not care for the food offered it. The animal rapidly went down hill and died on Nov. 3, 1940. Three differential counts made during the dysenteric stage averaged 3 per cent eosinophiles.

Autopsy findings: Body of an emaciated monkey with lumps of blood and mucus still plugging the anus. On opening the peritoneal cavity we found the small and large intestines to be distended, while the lower margin of the great omentum was partly adherent to the descending colon. The liver was markedly enlarged with a somewhat granular surface. The large intestine from the tip of the large appendix to the rectum was markedly congested, thickened and rough;

the small intestine was also congested. On opening the portal veins and its principal tributaries we obtained about 200 male and female adult worms. A few more were squeezed out from the cut surface of the liver which offered some resistance to cutting. The spleen was only slightly enlarged, its pulp bulging out to a certain extent on section. On opening the large intestine we saw the same pathological lesions both in character and extent observed in the first monkey. No visible ulcerations were found in the mucosa of the small intestine.

The heart and lungs were apparently normal except for a moderate degree of congestion. On opening the inferior vena cava we found two pairs of sexually mature flukes near its junction with the heart; and on exploring further into the right auricle with a glass pipette, a couple more of worms were aspirated. Toto histological sections of the heart revealed sections of adult males and females in undetermined number enmeshed in the fibrinous clot in the right ventricle. The uterus of the female worms was found full of eggs. Histological sections of the large intestine and liver showed lesions identical to what have been described in the first monkey. No eggs were found in the brain, kidney, spleen, and heart wall but a small number of them were found in the lung tissue.

COMMENTS

In the present paper reference to the other pathological findings will be omitted for future reports. Discussion will be restricted to the rather anomalous occurrence of several adult apparently egg-laying specimens of *S. japonicum* in the inferior vena cava and right chambers of the heart of two experimentally infected monkeys. As far as our knowledge of the literature on the subject goes this is the first report of adult specimens of *Schistosoma japonicum* occurring in the right chambers of the heart of its mammalian host. In 1921, Miyagawa and Takemoto [5] reported the finding of young schistosomes in the arterial system of animals experimentally infected with *S. japonicum* while Day [2] and Soroeu [6] recorded the finding of adult specimens of *Schistosoma mansoni* in the pulmonary artery and arterial vessels of some visceral organs respectively of man. A finding similar to that of Day in man was the reported presence

of a male *S. japonicum* in an artery of the lung of an experimental dog dying twenty-five days after infection (Faust and Meleney, 1924). Although these authors did not state whether the blood vessel involved was the pulmonary or the bronchial artery, we presume that they meant the former since to account for this anomalous occurrence they explained that "such a worm might have reached the lung either by leaving the portal system of veins through a pelvic anastomosis with the systemic veins and thence being carried through the vena cava to the heart and pulmonary artery, or it might have worked its way through the parynchyma of the liver to an hepatic vein and then reached the vena cava." When one of us (C.M.A.) visited the Tropen Institüt in Hamburg in June, 1939, his attention was invited by Professor Hans Vogel to an interesting reference concerning the unique finding of adult schistosomes in the coronary artery of a human autopsy case. Unfortunately for this report this reference was inadvertently lost, and as the present state of international relations is not so favorable for communication even for scientific purposes, this reference will have to be left out for the present.

These various reports including the present one may be considered to be of some significance since they indicate that in schistosoma infection adult worms may at times stray to anomalous locations in the body of the host wherein they may eventually carry their function of reproduction and egg deposition. The present finding, for instance, may help explain the relatively frequent presence of eggs of *S. japonicum* in the systemic area especially in the lung tissue of both man and experimental animals without the necessity of assuming that these ova originally came from the portal veins which is the normal parasitic habitat of this blood fluke. This possibility is admittedly greater in the case of either *S. mansoni* or *S. hematobium* since the natural parasitic habitats of these two schistosomes have a more direct anatomical connection with the internal iliac which drains into the inferior vena cava.

Although the more frequently reported presence of the eggs of *S. hematobium* and *S. mansoni* in the lung tissue can easily be explained by this anatomical connection, direct deposition of eggs in this locality can not be disregarded especially in the light

of the present finding. Faust and Meleney [3] think that the eggs of *S. japonicum* found in the lungs of man and experimental animals reached there from the liver. With the present finding of apparently sexually mature egg-laying adult specimens of *S. japonicum* in sufficiently large numbers in the inferior vena cava and right chambers of the heart such explanation, although retaining its validity, may no longer be necessary. Eggs directly deposited in the inferior vena cava, right chambers of the heart and pulmonary artery will naturally be in a more favorable situation to reach the left side of the general circulation for distribution in organs supplied by the systemic arteries than those in the portal veins, since they have to break through only the pulmonary barrier instead of both the liver and lungs. Faust and Meleney [3] say that it is difficult to understand how any great number of eggs of *S. japonicum* could break through the barrier of both liver and lungs to reach the arterial circulation and the brain. They give this as a reason for the relative rarity of the occurrence of *S. japonicum* eggs in the brain and other organs similarly located. However, in the short space of barely two years in the Philippines alone two autopsy cases, one of which had neurological manifestations in life, were noted with the eggs of *S. japonicum* in the cortex and other parts of the brain. One of these cases was already reported by Africa and Sta. Cruz [1] who found eggs of *S. japonicum* in histological sections of the brain, kidneys and heart besides those in the wall of the large intestine and liver. Several cases of schistosomiasis japonica with clear neurological manifestations such as epileptic seizures and convulsions have been observed in the charity wards of the Philippine General Hospital in recent years. More recently Garcia,[4] et al wrote on the occurrence of *S. japonicum* eggs in histological sections prepared from a piece of tissue extirpated from the wall of a phagedemic ulcer occurring on the anterior lower part of the left leg of a ten-year old Filipino girl from one of our endemic areas.

The fact that it was observed in two monkeys out of four in which dissection was done with meticulous care shows that, at least in the monkey, this condition cannot be regarded as rare. We may be able to verify or disprove this assertion by further experimentation. There seems to be no valid reason, at least

from the anatomical point of view, why this anomalous parasitism on the part of *S. japonicum* can not also happen in the human host. Divergence from this behavior in the human host, if such is found to be factual, may be better physiologically explained on the ground of host-parasite-relation. From the clinical point of view the present finding may also assume certain significance since such abnormal parasitism occurring in man may easily give rise to serious or fatal complications in the form of valvular occlusions or pulmonary infarctions.

As to how these adult worms happened to be lodged in the right chambers of the heart of our experimental monkeys, we agree with Faust and Meleney [3] in their explanation in connection with their own finding of a male *Schistosoma japonicum* in the lung of one of their experimental dogs previously mentioned that "such a worm might have reached the lung either by leaving the portal system of veins through a pelvic anastomosis with the systemic veins and hence being carried through the vena cava to the heart and pulmonary artery, or it might have worked its way through the parenchyma of the liver to an hepatic vein and thence reached the vena cava." We also agree with these authors that the former path is the most reasonable since it is difficult to understand how even the adolescent forms of the worm of the size of *S. japonicum* could successfully work their way through the interlobular venules, hepatic sinusoids, central venules and sublobular veins to reach the hepatic vein. In addition to these two possibilities a third one is worth considering. It is possible that some of the young developing schistosomula settled directly and developed to maturity in the vena cava and right chambers of the heart or in other similar localities without migrating to their normal parasitic habitat in the portal area as did the rest of their brood.

SUMMARY

A report is presented on two autopsies of monkeys experimentally infected with *Schistosoma japonicum* dealing principally with the unique finding in both animals of sexually mature male and apparently egg-laying female specimens of this human blood fluke in the inferior vena cava and right chambers

of the heart. A discussion of the possible parasitological and clinical significance of this unusual finding is included.

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PLATE I

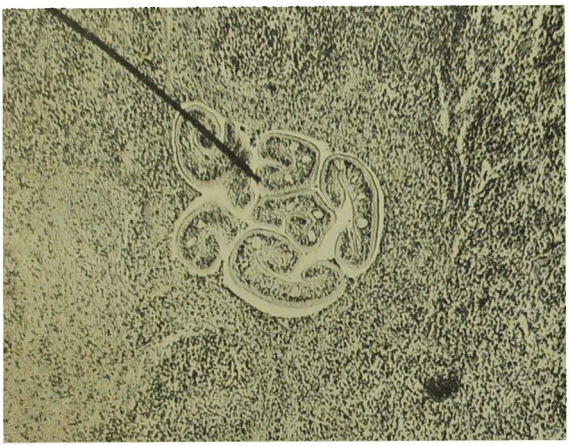

Fig. 1.—Histological section of a blood clot in the right ventricle of monkey 3 Sn showing cross sections of what appear to be several adult male specimens of *Schistosoma japonicum.* (× 50) The clot is already infiltrated with round cells and leucocytes.

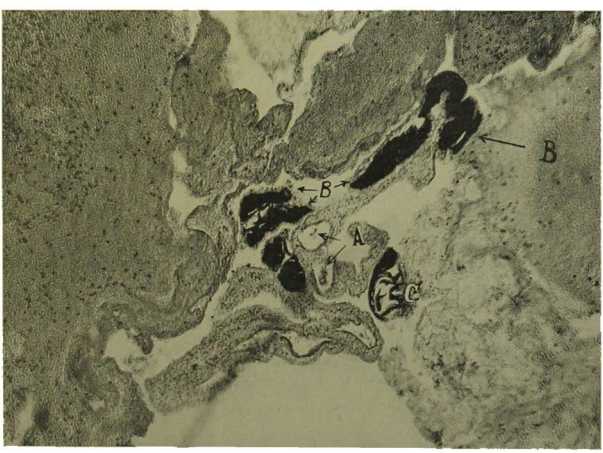

Fig. 2. Histological section of the same blood clot as above but higher up in the region of the tricuspid valve showing cross and tangential sections of male and female *Schistosoma japonicum.* (a) male, (b) female, (c) eggs, "en utero" (× 50)

PLATE II

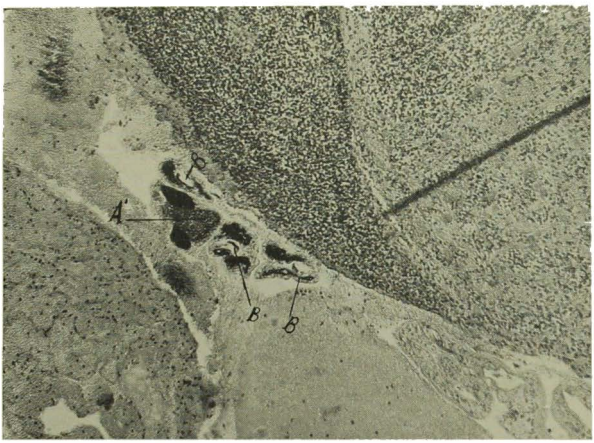

Fig. 1. Cross sections of female worms in histological sections from the same series as those appearing in plate I showing the ovary (a) and again eggs (b). (× 50)

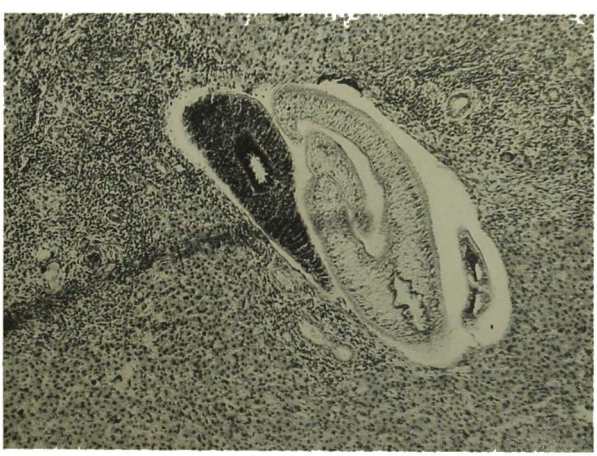

Fig. 2. Histological section of the liver of monkey 2 Re showing a cross section of a couple of *S. japonicum* inside what appears to be an interlobular venule. (× 50)

PLATE III

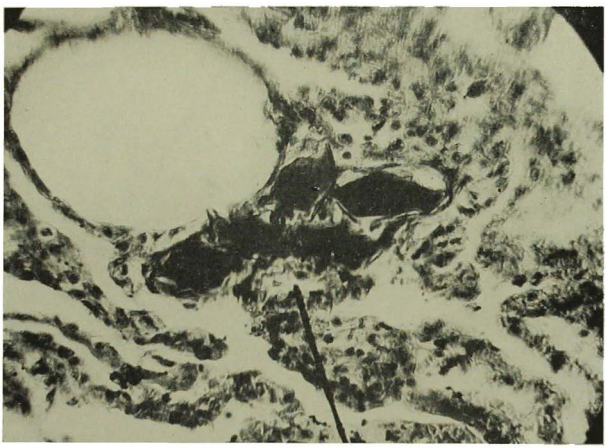

Fig. 1. Histological section of the lung of monkey 3 Sn showing five eggs of *Schistosoma japonicum* plugging a very well distended but still unruptured blood vessel beside an alveolar sac. (× 220)

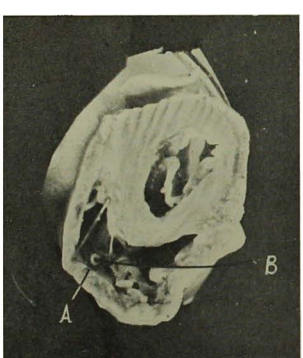

Fig. 2.—Gross transverse section of the heart of monkey 2 Re just below the tricuspid area showing an adult male worm (a) caught within the fibrin clot among the chorda tendinae. Note probe (b) thrust through the loop made by the worm. (1½ times natural size)

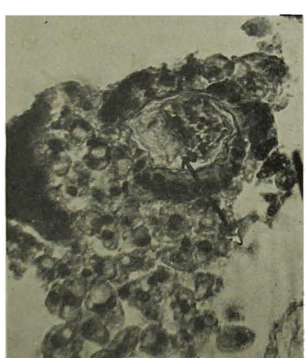

Fig. 3. An egg lying free in the auricular space intercepted by a giant cell. (× 220)

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(Signature) A. G. SISON

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FILOMENO PUMAREN
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Until December 31, 1941

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The ACTA MEDICA PHILIPPINA is devoted to the publication articles on any phase of medical science.

Manuscripts intended for publication in the ACTA MEDICA PHILIPPINA should be sent to the Chief Editor, ACTA MEDICA PHILIPPINA, College of Medicine, University of the Philippines, Manila.

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ACTA MEDICA PHILIPPINA

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The ACTA MEDICA PHILIPPINA is issued quarterly, one volume annually. The first volume begins with the July-September, 1939 number. The subscription rate for the Philippines and the United States is ₱4.00 Philippine Currency ($2.00 U. S. Currency). Single number, ₱1.50 ($.75). Regular postage charges will be made for subscriptions from foreign countries.

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